This Issue Exceeds 102,500 Copies

THE JOURNAL

OF THE

American Medical Association

Subscription, $8.00 | PUBLISHED WEEKLY | Single Copies, 25 Cents

VOLUME 115, No. 23

COPYRIGHT, 1940, BY AMERICAN MEDICAL ASSOCIATION

535 North Dearborn Street, Chicago, Ill.

DECEMBER 7, 1940

CONTENTS AND SUBJECT INDEX

The Surgical Correction of Horseshoe Kidney: Chairman's Address. F. E. B. Foley, M.D., St. Paul. 1945

Acute Ascending Paralysis. Russell N. DeJong, M.D., Ann Arbor. 1951

Polyradiculoneuritis. P. H. Garvey, M.D.; Nathaniel Jones, M.D., and Stafford L. Warren, M.D., Rochester, N. Y. 1955

Papers of Dr. DeJong and Drs. Garvey, Jones and Warren discussed by Drs. Casamajor, Bassoe, Ornsteen, Moersch, Bennett, Jolliffe, Bucy, Sands, Shaskan, Rabiner, Hayward, DeJong and Garvey.

Distention of Abdominal Viscera. N. C. Gilbert, M.D.; G. K. Fenn, M.D., and G. V. LeRoy, M.D., Chicago 1962

Discussed by Drs. Morrison, Greene and Miller.

Anuria Due to Sulfapyridine Calculi. Joseph F. Sadusk Jr., M.D.; Levin Waters, M.D., and Dwight Wilson, M.D., New Haven, Conn. 1968

Peripheral Neuropathy Due to Vitamin B_1 Deficiency in Diabetes Mellitus. Harry D. Fein, M.D.; Elaine P. Ralli, M.D., and Norman Jolliffe, M.D., New York 1973

The Coexistence of Brucella Infection and Hodgkin's Disease. N. B. Wise, M.D., and Mary A. Poston, M.A., Durham, N. C. 1976

Differential Diagnosis of Various Forms of Encephalitis. John A. Toomey, M.D., Cleveland 1985

CLINICAL NOTES

Use of Cellophane Cylinders for Desiccating Blood Plasma. F. W. Hartman, M.D., with the assistance of F. W. Hartman Jr., Detroit. 1989

SPECIAL ARTICLE

Glandular Physiology and Therapy: Introduction. Morris Fishbein, M.D., Chicago 1990

Relationship of Anterior Lobe of the Hypophysis to Other Endocrine Glands. Philip E. Smith, Ph.D., New York 1991

COUNCIL ON PHYSICAL THERAPY

Dangers Incident to Indiscriminate Use of Radium Compounds in Cutaneous Diseases. Anthony C. Cipollaro, M.D., New York. 1996

COUNCIL ON PHARMACY AND CHEMISTRY 1998

EDITORIALS

The A. M. A. Platform 2000

Life-Saving Service Without Recognition 2000

Selenium and Dietary Protein. 2001

CURRENT COMMENT

Teaching of Social Medicine 2001

The Post Has Never Seen a Vitamin! 2002

National Physicians' Committee. 2002

BUREAU OF LEGAL MEDICINE AND LEGISLATION 2022

(Subject Index on next page)

MEDICAL PREPAREDNESS

The 1940-1941 Training Program. 2003

Conference on Medical Preparedness Held November 23 2005

Army Reserve Officers Ordered to Active Duty 2009

ORGANIZATION SECTION

Official Notes 2010

A. M. A. SESSION CLEVELAND JUNE 2-6, 1941

SAUNDERS Christmas Shopping Plan

You could not give your professional friends Christmas Gifts that would be more acceptable, more lasting and more constantly helpful than SAUNDERS MEDICAL BOOKS.

And you will find Saunders *"Easy Shopping Plan"* a most convenient way of selecting and buying these Christmas Gifts. *The plan is very simple:* Just send us the names and addresses of those physicians to whom you wish books sent, indicating the Saunders Book you wish sent to each. We will then send the books direct, each with a note saying the gift is from you; or if you wish we will enclose your personal card.

The amount of your purchase may be charged to your account through our "Easy Payment Plan" of budgeting the amount over twelve monthly payments, with $3.00 as the smallest monthly payment. Or, you may make your purchases payable in 30, 60 or 90 days—just as you wish. *There are no carrying charges.*

On Page 3 today you will find a list of some of the current Saunders Book successes that will make ideal gifts for your doctor friends.

For a complete listing of Saunders Books, write today for our new Illustrated Catalogue. It will gladly be sent to you without charge.

See SAUNDERS GIFT SUGGESTIONS on Page 3

SUBJECT INDEX TO THIS ISSUE

The letters used to explain in which department the matter indexed appears are as follows: The Star (*) indicates an Original Article; "ab," abstract; "E," Editorial; "C," Correspondence; "Ml," Medicolegal; "ME," Medical Economics; "OS," Organization Section; "SS," Student Section.

A. M. A. Annual Congress on Medical Education and Licensure OS-2010
Committee on Medical Preparedness 2004; 2006
Conference on Medical Preparedness 2005
Acid, nicotinic, for sulfanilamide toxicity .. 2017
Adrenals, corticotropic hormone ... *1993; *1995
pituitary relationship *1995
"Alkali disease" of farm animals E-2001
Allergy, sensitivity to soap 2018
Ambulance duty, men nurses for C-2016
American Association for Study of Neoplastic Diseases 2013
Medical Association of Vienna C-2016
Rheumatism Association; proceedings 2023
Androgen treatment of hypogonadism 2017
Anemia, hemolytic, in infants ab-2027
infantile constitutional ab-2032
Angina Pectoris, effect of flatulence *1962
Anteron 1998
Army, U. S., military training program .. *2003
U. S., reserve officers ordered to active duty 2009
Arteries, coronary circulation, effect of flatulence on *1962
Arteriosclerosis, no arteries exempt 2018
Arthritis, mono-articular and pauciarticular, in children ab-2023
procaine injections for ab-2025
Association News 2010
Asthma, action of choline derivatives ab-2031
Atropine prevents anginal attack *1962
Australian X Disease, diagnosis *1985
Ballin Memorial Lectures 2012
Blood, hypoprothrombinemia of newborn .. ab-2032
plasma, cellophane cylinders to desiccate . *1989
transfusion, American vans in England .. 2014
transfusion, collecting blood for 2009
Board Examinations 2019
Book Notices 2020
Books Received ..... Adv. page 42
Brachial Plexus block for shoulder pain .. ab-2025
Brain disease, classification *1985
Bureau of Legal Medicine and Legislation . 2022
Bursitis, subdeltoid, procaine injection .. ab-2025
Carbohydrate metabolism and pituitary *1993
Cellophane cylinders for desiccating plasma . *1989
Cerebrospinal fluid in encephalitis *1987
protein in polyradiculoneuritis . *1955; ab-1960
Chiropractic: meningitis; death of patient Ml-2022
Cleveland's Health Museum opened 2012
Cod Liver Oil for psoriasis ab-2028
Coitus, vulva tuberculosis caused by ab-2032
College of Physicians of Philadelphia 2013
Cornea, preserved, homotransplantation .. ab-2027
Correspondence 2016
Council on Pharmacy and Chemistry 1998
Council on Physical Therapy 1996
Deaths 2015
De Lamar Lectures 2011
Diabetes Mellitus, peripheral neuropathy from vitamin B_1 deficiency *1973
Diving, life-saving service of U. S. Navy . E-2000
Drugs in Great Britain C-2016
Ductus Arteriosus, patent, endarteritis complicating ab-2029
Eating, anginal attack after *1962
Encephalitis, differential diagnosis *1985
Encephalomyelitis, equine, diagnosis *1985
Endarteritis, bacterial, in patent ductus arteriosus ab-2029
Endocrine Glands-pituitary relationship *1991
Endocrinology, Squibb award 2013
Erdheim, Jacob, tribute to C-2016
European War, meningitis in ab-2031
American vans for transfusion 2014
Britain's health improves 2014
casualties from bombing of civilian population 2014
London hospitals carry on 2014
Fat metabolism and anterior pituitary *1993
Fever, therapeutic; polyradiculoneuritis after *1955; ab-1960
Fingers, Heberden's nodes ab-2024
Flatulence, effect on coronary blood flow .. *1962
Football, deaths from, decline 2013
Foreign Letters 2014
Formaldehyde, industrial poisoning 2017
Gately, G. L., new health commissioner 2011
Gentian Violet, nausea and vomiting from .. 2017
GLANDULAR PHYSIOLOGY AND THERAPY ... *1990
Goiter, Exophthalmic, liver function in . ab-2031
Gonadin 1998
Gonadogen 1998
Gonadotropins, complex *1992
pregnant mare serum 1998
treatment of hypogonadism 2017
Gonads, hypogonadism in young boy, androgens and gonadotropins for 2017
-hypophysis relationship *1995
Growth hormone *1992
Guillain-Barré Syndrome after sulfanilamide and fever therapy *1955; ab-1960
Hair excessive, radium for *1997
Health, Cleveland's Museum opened 2012
commissioner, new, Dr. Gately 2011
improves under war conditions, England .. 2014
program of N Y A 2008
Heberden's nodes ab-2024
Hemolysis disease in infants ab-2027
Hospitals, beds, military training program .. 2003
carry on, London 2014
new ones opened, Ore. 2013
U. S. Army, staff personnel 2009
Industrial formaldehyde poisoning 2017
N Y A to examine employees 2012
physicians questionnaires 2006
Infants, hemolytic disease in ab-2027
newborn, hypoprothrombinemia ab-2032
syphilitic mother nurse baby? 2018
Insurance, health, propaganda in colleges . E-2001
Interns and the draft 2008
Jaundice, hemolytic, in infants ab-2027
hepatic function in ab-2027
Kaufmann, Rudolph, tribute to C-2016
Keloids, radium treatment *1997
Kidneys, horseshoe, symphysiotomy with nephropexy for *1945
Laboratory, fee schedule 2007
Lactation hormone *1993
syphilis of mother 2018
Licensure, Annual Congress on OS-2010
changes in status 2013
Liver extract injection or orally? 2018
function in icterus gravis ab-2027
function in thyrotoxicosis ab-2031
Lymphogranuloma, Brucella cause? *1976
Malpractice: municipality; liability Ml-2023
Marriages 2014
Mecholyl, action in asthma ab-2031
Medical Education, A. M. A. Annual Congress on OS-2010
course on chest diseases, New York 2012
Medical Examinations and Licensure 2019
Medical Preparedness 2003
Medical Preparedness, A. M. A. Conference on 2005
College of Physicians of Philadelphia program on 2013
Health Preparedness Committee, New York . 2012
1940-1941 military training program 2003
symposium on, Los Angeles 2011
Medical Service, communities deprived of .. 2007
National Physicians' Committee for Extension of E-2002
Medicolegal Abstracts 2022
Meetings, Coming Meetings 2023
Men nurses for ambulance duty C-2016
Meningitis, diagnosis (differential) *1985
in soldiers, benzylsulfanilamide and sulfapyridine for ab-2031
Menstruation disorders, mare serum gonadotropin for 1998
frequent, in girl aged 15 2018
Meyer, Theodore, tribute to C-2016
Mycosis fungoides, radium treatment *1997
National Physicians' Committee for Extension of Medical Service E-2002
Youth Administration 2008; 2012
Naturopathic physicians, Inc. 2012
Navy, U. S., life-saving service and the *Squalus* E-2000
U. S., officers ordered to active duty 2009
Nerves, vagus section effect on anginal attacks *1962
Neumann, Wilhelm, tribute to C-2016
Neuritis, polyneuritis of pregnancy 2018
polyradiculoneuritis after sulfanilamide and fever therapy *1955; ab-1960
Neuropathy, peripheral, in diabetic *1973
Nevi, radium treatment *1997
New and Nonofficial Remedies 1999
News 2011
North Dakota Naturopathic Physicians, Inc .. 2012
Northwestern University, gifts to 2011
Nurses, men, for ambulance duty C-2016
Organization Section 2010
Ovulation induced with mare serum gonadotropin 1998
Oxyuriasis, gentian violet for, nausea after . 2017
Pacific States Medical Executives' Conference 2013
Pal, Jacob, tribute to C-2016
Paralysis, acute ascending *1951; ab-1960
Physicians, in military training program ... 2003
National Physicians' Committee for Extension of Medical Service E-2002
ordered to active duty 2004; 2009
practice, protecting those in service 2008
schedules, remarks on 2005; 2006
Pituitary, anterior, relationship to other endocrine glands *1991
thyrotropic hormone *1992
Polioencephalomyelitis, diagnosis *1985
Polycythaemia vera, venesection and roentgen rays for 2018
Porter, Joseph, memorial 2011
Pregnancy, polyneuritis of; thiamine and liver extract for 2018
Procaine injections for painful shoulder . ab-2025
Protein, relation to selenium E-2001
Psoriasis, vitamin D preparation for ab-2028
Psychiatry, Maryland Society 2011
Pennsylvania Society 2013
Puerto Rico Medical Association 2013
Pyelo-ureteritis from sulfapyridine *1968
Queries and Minor Notes 2017
Radio Broadcasts 2010
Radium, indiscriminate use *1996
Radon, indiscriminate use *1996
Rheumatism, American Rheumatism Association 2023
Roentgen examination of drafted men . 2007; 2012
Rothberger, Charles F., tribute to C-2016
Saturday Evening Post has never seen a vitamin E-2002
Schilder's Disease, diagnosis *1985
Sclerosis, acute multiple, diagnosis *1985
Selenium and dietary protein E-2001
Shoulder conditions, analgesic injections . ab-2025
Skin diseases, indiscriminate radium therapy *1996
sensitive, soap substitutes for 2018
Smallpox outbreak, Mich. 2012
Soap substitutes for sensitive skin 2018
Social medicine, teaching in colleges E-2001
Society Proceedings 2023
Spine intervertebral disk, narrowed ab-2032
Squalus, life-saving service of Navy E-2000
Squibb award in endocrinology 2013
State Board Examinations 2019
Sterility treatment, mare gonadotropin for . 1998
Stomach cancer masquerading as benign . ab-2030
Students, medical, and the draft 2008
Sulfanilamide, benzylsulfanilamide for meningitis ab-2031
polyradiculoneuritis after *1955; ab-1960
toxic symptoms, nicotinic acid for 2017
treatment of trachoma ab-2032
Sulfapyridine calculi, anuria due to *1968
treatment of meningitis in soldiers ab-2031
Symphysiotomy for horseshoe kidney *1945
Syphilis of mother, nursing and continued treatment 2018
rejecting registrants 2007
Testis, undescended, mare gonadotropin for . 1998
Thiamine hydrochloride treatment of diabetic peripheral neuropathy *1973
Thorax, course on chest diseases, N. Y. 2012
Thyroid and hypophysis relationship *1995
enlarged, in girl aged 15 2018
Tonics and Sedatives ..... Adv. page 36
Trachoma, sulfanilamide for ab-2032
Tuberculosis: as an occupational disease . Ml-2022
conjugal ab-2032
pulmonary, extrapleural pneumothorax . ab-2029
pulmonary, lobectomy and pneumonectomy in ab-2029
Tumors, American Association for Study of . 2013
Typhus vaccines: Weigl; Wohlrab 2018
Undulant Fever and Hodgkin's disease ... *1976
vaccinate humans? 2017
University, health insurance propaganda? . E-2001
Urine, anuria from sulfapyridine calculi .. *1968
Venereal Disease, rejecting registrants 2007
Venesection in polycythaemia vera 2018
Viscera, abdominal, distention, and angina . *1962
Vitamin B_1 deficiency in diabetes *1973
B_1 injection or orally 2018
B_1, relation to polyneuritis after fever therapy ab-1961
D preparations for psoriasis ab-2028
K, hypoprothrombinemia of newborn .. ab-2032
Saturday Evening Post advertisement .. E-2002
Vulva, tuberculosis from coitus ab-2032
Wagner-Jauregg, Julius, tribute to C-2016
Wenckebach, Karel F., tribute to C-2016
Winterberg, Heinrich, tribute to C-2016

THE JOURNAL of the American Medical Association is published weekly by the American Medical Association, 535 North Dearborn Street, Chicago, Ill. Subscription price, $8.00 a year. 25c a copy. Canadian $9.50. Foreign $12.00. Entered as second class matter June 25, 1885, at the Postoffice at Chicago, Ill., under Act of March 3, 1879.

BOOK BUYING SIMPLIFIED
We supply new and standard medical works of all publishers
ONE ORDER—ONE REMITTANCE
GET OUR LATEST BULLETIN
CHICAGO MEDICAL BOOK CO. 438 S. Honore St. CHICAGO

The Journal of the American Medical Association

Published Under the Auspices of the Board of Trustees

VOL. 115, No. 23 COPYRIGHT, 1940, BY AMERICAN MEDICAL ASSOCIATION CHICAGO, ILLINOIS DECEMBER 7, 1940

SURGICAL CORRECTION OF HORSESHOE KIDNEY

CHAIRMAN'S ADDRESS

FREDERIC E. B. FOLEY, M.D.

ST. PAUL

The anomaly horseshoe kidney, apart altogether from accompanying renal pathologic change, presents a clearcut and definite clinical problem. It is the problem of what may be called horseshoe kidney disease as distinct from disease of the horseshoe kidney.

The literature abounds in reports of the occurrence of the anomaly horseshoe kidney and in descriptions of its morphology and autogenesis. There is an abundance of clinical reports dealing with disease of the horseshoe kidney. They recount occurrence of all the ordinary renal lesions such as hydronephrosis, pyonephrosis, stone, tuberculosis and neoplasm, found in association with this extraordinary form of kidney. Some of the reports speculate concerning the anomaly as an etiologic factor in occurrence of the associated lesion. In all but a few reports, to be mentioned in detail later, the anomaly has not been held directly responsible for the symptoms present and no attempt has been made to eliminate it as an etiologic factor by restoration of normal anatomic relationships. They are simply reported cases of common renal lesions occurring in an uncommon anomalous kidney. Such cases do not touch on the clinical problem of the anomaly itself—that is, the problem of relieving the painful and other symptoms caused by the anomaly and preventing or arresting pathologic changes that may insidiously accompany it.

A horseshoe kidney not affected by any significant pathologic change apart from the anomaly may be productive of symptoms demanding relief. With the exception of only a few reported cases, surgeons have failed to accord this relief and apparently have failed to contemplate the surgical problem of doing so. It will be shown by the personal cases here reported and by analysis of other cases reported in the literature that surgical correction of the anomaly by division of the isthmus and nephropexy on one or both sides is capable of restoring normal relationships and relieving the subjective symptoms that may be caused by the anomaly.

With the exception of twelve cases reported prior to 1930, when the present thesis had its inception, and six cases reported since then, all clinical reports have neglected this particular and very important phase of horseshoe kidney disease. This cannot be said of Gutierrez's monograph "The Clinical Management of Horseshoe Kidney,"[1] published in 1934. Gutierrez originated the term "horseshoe kidney disease" to distinguish cases of the anomaly not associated with significant pathologic change from cases in which concomitant disease of the malformed kidney is present. It is a useful and descriptive term and should be retained.

Although not supported by the results of personal experience, Gutierrez concluded that horseshoe kidney per se without any accompanying renal lesion of significance is capable of causing subjective symptoms and that these should be amenable to relief through surgical restoration of normal relations—that is, operative division of the fused kidneys and their restoration to normal positions.

Prior to Gutierrez's publication in 1934 I had already embarked on the same thesis by another avenue—trial of the operation. In 1935 a preliminary report[2] described the early results of this operation in five cases in which there was no significant pathologic change apart from some degree of the pelvic dilatation that usually accompanies the anomaly. The present address as chairman of your section will report my personal experience with this procedure in seven such cases, recount the end results in them and indicate the conclusions that may be drawn from them and the nineteen similar cases reported in the literature.

Any outspoken pathologic change in the horseshoe kidney that is wholly responsible for the symptoms present provides the same clearcut and definite indications for correction of the lesion that the same lesion would provide in the normally formed kidney. As already indicated, such cases of horseshoe kidney associated with outspoken pathologic change do not enter the present considerations. However, with few exceptions reports in the literature indicate that in the consideration and management of horseshoe kidney the associated lesion has merely been assumed to be wholly responsible, has overshadowed the anomaly and has been the sole object of clinical attention and surgical attack, while the anomaly itself and its evils have been almost wholly neglected. This does not prove or admit that in such cases the anomaly is not just as important as the common renal lesion accompanying it or even that the anomaly may not have been responsible for development of the lesion present. To distinguish between cause and effect in any relationship that exists between the anomaly and the lesion associated with it is not my purpose here. The thesis deals only with horseshoe kidney per se as a clinical problem and does not touch on the problems presented by concomitant pathologic change.

Dr. Harry A. Wilmer rendered assistance in the search for references and prepared the accompanying bibliography and case summaries.

Read before the Section on Urology at the Ninety-First Annual Session of the American Medical Association, New York, June 13, 1940.

1. Gutierrez, Robert: The Clinical Management of Horseshoe Kidney, New York, Paul B. Hoeber, Inc., 1934.
2. Foley, F. E. B.: Minnesota Med. **18**: 176-182 (March) 1935.

THREE GROUPS OF CASES OF HORSESHOE KIDNEY

For the present purpose all cases of horseshoe kidney may be divided into three groups and commented on as follows:

GROUP 1.—*Cases of horseshoe kidney without renal pathologic change or symptoms of renal origin.* In the majority of clinically recognized cases belonging to this group the urologic investigation leading to discovery of the anomaly is prompted by painful abdominal symptoms of other than renal origin. In a large minority of cases the investigation is prompted by the patient's own discovery of an abdominal mass representing the isthmus of the horseshoe kidney or by the physician's similar discovery. In a small minority of cases belonging to this group the coincidence of urinary symptoms of vesical or urethral origin, not related to the upper

TABLE 1.—*Summary of Cases of Symphysiotomy for Horseshoe Kidney Reported in the Literature*

Case	Author and Year	Sex, Age	Clinical Data	Operation	Comment
1	Martinow,[3] 1910	♀ 49	Pulsating sensation in abdomen since childhood; pain above umbilicus of 4 years' duration; constipation; severity and frequency of pain increased; palpable mass	Chloroform anesthesia; transperitoneal approach; tumor found to represent horseshoe kidney; isthmus separated from aorta and divided; kidneys separated	Diagnosis by palpation: result, 5 months' complete relief
2	Rovsing,[3] 1911	♂ 23	Lower abdominal pain for 5 years occurring in attacks of sudden onset and lasting 3 hours; all attacks induced by activity; palpable mass moving with respiration	Transperitoneal approach; isthmus divided; separated left kidney retracted into normal position	Diagnosis by palpation under anesthesia: result, early complete relief
3	Malinowsky,[3] 1912	♀ 28	Persistent abdominal pain; hyperacidity; palpable mass	"Isthmus crushed"	Complete relief of pain; hyperacidity not relieved: result, early complete relief
4	Brongersma,[3] 1914	♀ 37	Since childhood bilateral lumbar pain more severe on left; later lower abdominal pain; left-sided colic; 2 attacks of bilateral pyelitis treated by lavage; previous operation for calculus; calculus not found; uterus and tubes removed	Transperitoneal approach; isthmus divided; kidneys retracted from midline	Result, 2 months "felt well"
5	Brongersma,[3] 1919	♂ ?	Pain in region of umbilicus; hematuria on 1 occasion following heavy lifting	Transperitoneal approach; isthmus divided; urinary fistula treated by nephrostomy	Diagnosis by operation: result early complete relief,
6	Kroiss,[3] 1922	♀ 29	Attacks of severe abdominal pain for 19 years; severe bilateral lumbar pain radiating to umbilicus occasioned by heavy lifting; pain relieved by flexion of spine, increased by lifting, coughing and sneezing	Transperitoneal approach; isthmus resected	Result, permanent complete relief
7	deGroot,[3] 1922	♂ 16	Attacks of abdominal pain of increasing severity 2 years; palpable mass	Transperitoneal approach; isthmus divided	Result, "recovery"
8	van Houtum,[3] 1922	♀ 37	Attacks of severe colicky lumbar and abdominal pain 1½ years; hematuria: pain and hematuria induced by exercise disappeared on rest; diagnosis by palpation under anesthesia, confirmed by pyelography	Transperitoneal approach; isthmus divided	Result, permanent relief
9	Kidd,[3] 1922	♀ 32	Lumbosacral pain in increasing severity for 4 years; pain increased by exercise; also occurred when lying down; partially relieved by lying on right side; previous operation with discovery of horseshoe kidney	Transperitoneal approach (3 months following previous operation); tense isthmus lying against aorta; isthmus divided; both kidneys retracted	Result, postoperative death on 5th day
10	Judd, Braasch and Scholl,[4] 1922	♀ ?	Not stated	Hydronephrosis; "... isthmus was divided and the diseased kidney rotated in order to permit the ureter to lie in normal position"	Result, 18 years of complete relief (personal communication)
11	Eggers,[3] 1922	♂ 18	Former period of vague right-sided pain of 10 years' duration followed by relief; 12 weeks prior to observation, sudden attacks of severe left-sided colic followed by passage of stone; recurrence of pain; palpable mass	"Left flank incision"; removal of stone; isthmus divided; left nephropexy	Diagnosis by operation: result, "recovery"
12	Papin,[3] 1922	♀ 32	Lumbar and abdominal pain of gradually increasing severity; palpable mass; diagnosis by pyelography	Extraperitoneal approach; division of isthmus	Result, early complete relief
13	Mintz,[3] 1925	♀ 33	Recurrent attacks of poorly localized pain; large palpable mass	Transperitoneal approach; division of isthmus	Diagnosis by operation: result, early complete relief
14	Lynch and Thompson,[5] 1934	♂ 36	"Backache" and pain referable to left kidney; relieved by lying down; pain referable to both kidneys of increasing severity for 15 days; tenderness in both flanks	Retroperitoneal approach; division of isthmus; division of anomalous vessels	Diagnosis by pyelography (?): complete relief of left-sided pain; right-sided pain improved: result, 3 months as noted
15	Chwalla,[5] 1935	♀ 29	Bilateral lumbar and umbilical region pain induced by heavy lifting of 4 years' duration; "abdominal colic" since childhood, recently more frequent; loss of appetite; pulsation in umbilical region; slept in semierect position for relief of pain	Transperitoneal approach; resection of isthmus	Result, 14 years of complete relief
16	Chwalla,[5] 1935	♀ 31	Abdominal and lumbar pain since childhood induced by extension of spine; attacks of great severity; palpable, very movable mass identified as horseshoe kidney	Transperitoneal approach; division of isthmus	Diagnosis by pyelography (?): result, 10 years of complete relief
17	Baker and Colston,[5] 1936	♂ 30	Intermittent right lumbar pain for 7 years, relieved by lying down	Extraperitoneal approach; division of isthmus; right nephropexy	Result, early complete relief
18	Baker and Colston,[5] 1936	♂ 52	Attacks of severe right lower quadrant pain for 1 year; right renal calculus	Extraperitoneal approach; division of isthmus; right pelviolithotomy; right nephropexy	Diagnosis by pyelography: result, early complete relief
19	Strode,[5] 1939	♂ 25	Abdominal pain for 6 years; tenderness in left kidney region; appendectomy 3 years previously without relief	1. November 1936, left retroperitoneal approach; division of isthmus; left nephropexy 2. November 1937, right retroperitoneal approach; resection of lower pole of right kidney; right nephropexy (?)	Diagnosis by pyelography: result, early complete relief

urinary tract, has indicated the urologic investigation leading to discovery of the anomaly.

In cases of this group the horseshoe kidney is of clinical importance only in a negative way. Since it is not affected by pathologic change and causes no symptoms, there is no more reason for surgical intervention with such a horseshoe kidney than there is reason to intervene surgically with an undiseased and symptomless kidney of normal form. The anomaly itself is of no surgical importance. In this group of cases the clinical burden is to discover the nonrenal cause of symptoms, if symptoms are present, and avoid the error, and possibly needless surgery, of assigning the anomalous though innocent horseshoe kidney as the cause of symptoms.

GROUP 2.—*Cases of horseshoe kidney with outspoken renal pathologic change and symptoms of renal origin.* Under competent medical care and modern methods of urologic diagnosis most cases of this group are clinically recognized, both the anomaly and associated lesion being clearly demonstrated. In most cases the associated lesion presents the same diagnostic and surgical problems that the same lesion would present in the normally formed kidney. These problems are made peculiar by presence of the anomaly, but the importance the anomaly may have beyond this has been largely neglected. A large majority of the reported cases of horseshoe kidney belong to this group. The associated lesions have been of great variety and include almost all of the common surgical renal lesions such as hydronephrosis, pyonephrosis, stone and tuberculosis.

In many cases of this group surgical correction of the "common renal lesion" associated with the anomaly is only one part of the problem present. Often it is found that correction of the lesion associated with the anomaly does not serve completely to right the evil. If the anomaly has been an etiologic factor in occurrence of the lesion its continuing presence may lead to recurrence of the lesion. If the symptoms have been due wholly or partly to the anomalous relationships they will not be completely relieved without surgical correction of the anomaly. Conceivably hydronephrosis occurring in association with horseshoe kidney may not be due to mechanical obstruction occasioned directly by the anomaly but instead to stricture, aberrant vessel or other form of obstruction not caused by the anomaly. Surgical correction of such an obstruction without correction of the anomaly should give complete relief provided the anomaly per se plays no part in the production of symptoms. The fact is, however, that most cases of hydronephrosis occurring in association with horseshoe kidney are due directly to mechanical obstruction made by the horseshoe kidney itself. This type of obstruction will be further considered in the comments concerning the cases of group 3.

In many cases of this group an unsatisfactory result of operation is recognized but there has been habitual failure to recognize that continuing presence of the anomalous relations and failure to correct them surgically are responsible for the unsatisfactory outcome.

In this combination of an outspoken renal lesion associated with horseshoe kidney it may be difficult or impossible to say what part of the symptom complex is caused by the lesion and what part is caused by the anomaly. Unless there are good indications to the contrary, it may be best in such cases to proceed on the assumption that the associated lesion is solely responsible, surgically correct it and leave the anomalous relationships undisturbed. Should an unsatisfactory result ensue, the responsibility of the anomaly for it should be investigated, and if good indications are found the anomalous relationships should be corrected by division of the isthmus and normal positioning of the separated kidneys.

GROUP 3.—*Cases of horseshoe kidney with symptoms of renal origin but without renal pathologic change other than some degree of pelvic dilatation.* The cases of this group are the ones most intimately concerned in the present thesis.

There is good reason to believe that a large number of cases of horseshoe kidney belong to this group—and yet with few exceptions nothing has been done about them. They have been nearly like the weather: every one talks about the weather but no one does anything about it.

Many cases of horseshoe kidney with pyelograms showing no significant departure from normal except for the anomaly are recognized clinically and many of them have been reported. They may belong to group 1, in which the anomaly is not the cause of pain or any other clinical manifestations whatever. As already indicated, such cases are of no clinical importance. However, in many cases belonging to this group the malformation itself is directly the cause of pain and other symptoms, which prompt investigation, leading to discovery of the anomaly.

If symptoms are present, the burden of proof goes with saying they are not caused by the horseshoe kidney. This is particularly true when the symptoms are suggestive or typical of renal origin. However, it appears that the horseshoe kidney without any significant pathologic change may cause vague and indefinite symptoms not suggestive, and by no means typical, of renal origin. Gutierrez emphasizes this point. Among these symptoms are vague abdominal pain or "belly ache," constipation and other digestive disturbances.

From personal experience I am not familiar with such cases, for in all the cases here reported in support of the present thesis symptoms typical of renal origin were present.

Nor can I say from personal experience that absence of significant pathologic change properly defines this group of cases. In some of the cases here reported there was obvious pathologic change in the form of pelvic dilatation while in others the pyelogram after operation has shown disappearance of what was originally considered insignificant dilatation of the pelvis in the preoperative pyelogram. In the light of this change in response to operation it becomes obvious that the slight dilatation present before operation in these cases actually should have been regarded as significant.

My own observations in the personal cases here reported make it appear certain that the various degrees of pelvic dilatation usually present in cases of this group are due directly to mechanical obstruction of the ureters occasioned by the anomaly: abnormal insertion of the ureter into the pelvis and contact of the ureter with the isthmus. These malrelationships were clearly evident in every case. The pelvic dilatation present varied from insignificant dilatation to outspoken hydronephrosis (case 5). Even in the latter case no other possible cause of obstruction could be found. The

dilatation, whatever its degree, regularly diminished in response to surgical restoration of normal relationships of the ureter.

However, in the literature and particularly in the monograph of Gutierrez are found reports of cases with

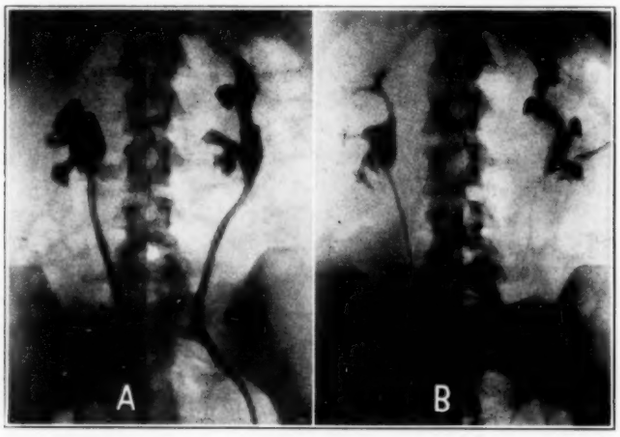


Fig. 1 (case 1).—*A*, preoperative right and left pyelo-ureterograms; *B*, postoperative right and left pyelo-ureterograms.

pyelograms showing no deformity whatever suggestive of pathologic change apart from the anomaly but presenting either symptoms typical of renal origin or vague symptoms possibly of renal origin. To determine surgical indications, if any, in the latter cases is a difficult problem. If comprehensive investigation fails to disclose an extrarenal lesion capable of causing the vague symptoms then there is much reason to believe that the symptoms will be relieved by correction of the anomalous relations, by division of the isthmus and nephropexy on one or both sides.

PROPER CLINICAL MANAGEMENT OF HORSESHOE KIDNEY

In the foregoing discussion a problem concerning the clinical management of horseshoe kidney has been posed. The comments made anent the matter already

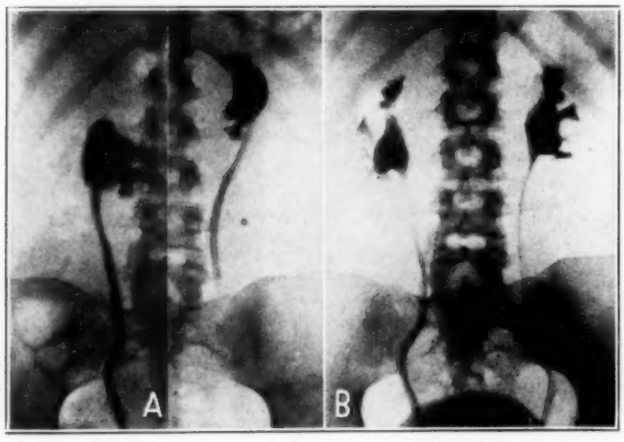


Fig. 2 (case 2).—*A*, preoperative right and left pyelo-ureterograms; *B*, postoperative bilateral pyelogram.

have indicated the chief conclusion to be drawn. That conclusion is:

The anomaly horseshoe kidney not affected by concomitant pathologic change of significance may be productive of painful and other symptoms and insidious development of renal disease and can be restored to normal anatomic relations with relief of symptoms and arrest of the insidiously developing renal disease by appropriate surgical intervention—symphysiotomy and nephropexy.

This conclusion is based on cases reported in the literature and the personal cases to be reported here.

Prior to 1930 when the first personal case was encountered there had been reported in the literature only twelve cases of horseshoe kidney in which symphysiotomy with or without nephropexy had been made.[3] All of these were in Europe and in all save one, the case of Papin, operation by the transperitoneal approach was done. Unfortunately the eventual end results in these cases are not described, but the immediate symptomatic result was reported as excellent in all of the eleven surviving patients.

In a paper dealing with renal anomalies in general published in 1922, Judd, Braasch and Scholl [4] mention but do not otherwise report a case of horseshoe kidney in which the isthmus was divided and "the right portion of the divided kidney was rotated in such a way as to make the ureter lie in its normal position." By personal communication it is learned from Dr. Braasch

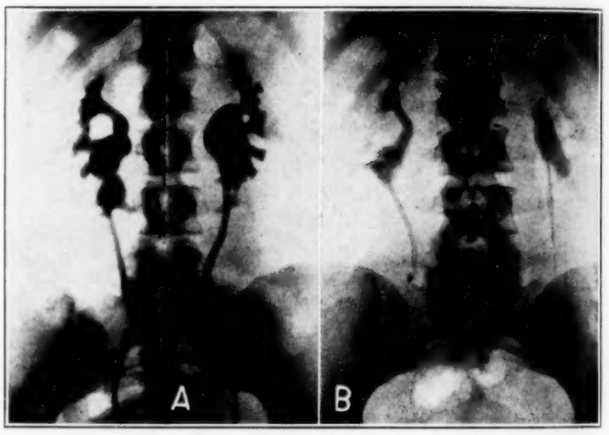


Fig. 3 (case 3).—*A*, preoperative right and left pyelo-ureterograms; *B*, postoperative excretion urogram.

that eighteen years after operation this patient was alive and well, the result of operation appearing to be excellent.

The twelve European cases and the case of Judd, Braasch and Scholl, all reported prior to 1930, appear as cases 1 to 13 inclusive in the cases of symphysiotomy for horseshoe kidney reported in the literature summarized in table 1.

Since 1930, when the series of personal cases was started, there have been reported in the literature six more cases of this sort.[5] The results in three cases are

3. The twelve cases were reported by:
Martinow, A.: Zentralbl. f. Chir. **9**: 314, 1910.
Rovsing, Thorkild: Ztschr. f. Urol. **5**: 587-601, 1911.
Malinowsky: J. d'urol. **1**: 869, 1912.
Brongersma, H.: Ztschr. f. Urol. **8**: 470, 1914.
Brongersma, H.: J. d'urol. **8**: 425, 1919.
Kroiss: Verhandl. d. deutsch. Gesellsch. f. Urol., 1922.
deGroot, S. B.: Ztschr. f. urol. Chir. **8**: 170, 1922.
van Houtum, G., ibid. **8**: 165-169, 1922.
Kidd, Francis: Proc. Roy. Soc. Med. (Sect. Urol.) **15**: 52-54 (Aug.) 1922.
Eggers, H.: Ztschr. f. urol. Chir. **9**: 427-432, 1922.
Papin, Edmond: Assoc. franç. d'urol., Proc.-Verb. **22**: 557, 1922.
Mintz: Khir. Arkh. Veliaminova **29**: 1047, 1923, cited by Papin, Edmond: Arch. d. mal. d. reins **2**: 24, 1925.

4. Judd, E. S.; Braasch, W. F., and Scholl, A. J.: Horseshoe Kidney, J. A. M. A. **79**: 1189-1196 (Oct. 7) 1922.

5. Lynch, K. D., and Thompson, R. F.: Urol. & Cutan. Rev. **38**: 239-242 (April) 1934. Chwalla, R.: Arch. f. klin. Chir. **183**: 590-598, 1935. Baker, W. W., and Colston, J. A. C.: J. Urol. **35**: 264-288 (March) 1936. Strode, J. E., ibid. **41**: 285-293 (March) 1939.

stated to be excellent eight years, ten years and fourteen years after operation. In the remaining three cases only the immediate result is stated but this was excellent in all. These six cases reported since 1930 appear as cases 14 to 19 inclusive in table 1.

My six cases of horseshoe kidney and one case of unilateral fused kidney corrected by symphysiotomy and nephropexy on one or both sides, together with the nineteen cases reported in the literature, make a total of twenty-six cases for use in appraising division of the isthmus and nephropexy in cases of fusion anomaly.

My six personal cases are reported in summary and illustrated as follows:

REPORT OF CASES

CASE 1.—This case, from the urologic service of the Ancker Hospital, was originally reported in 1932 by my associate in the service, Philip F. Donohue.[6]

A woman aged 32 had had pain in the right lower quadrant of the abdomen for twelve years. A mass to represent the isthmus was not palpable. Pyelograms (fig. 1 *A*) had the typical features of horseshoe kidney: low position, long axis oblique toward the midline below and medial direction of the inferior calices. There was slight dilatation of the pelves.

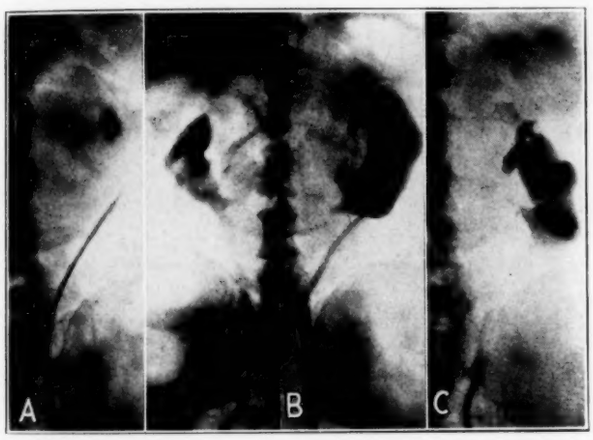


Fig. 4 (case 4).—*A*, preoperative urinary tract roentgenogram (left half; opaque catheter in ureter); *B*, preoperative right and left pyelo-ureterograms; *C*, postoperative left pyelo-ureterogram.

In March 1930, through a right flank incision, extraperitoneal exposure of the right half of the horseshoe kidney was made. The isthmus was divided and a right nephropexy was done. The operation gave complete and permanent relief of the right-sided pain.

Eight months after the operation the patient began to have pain on the left side exactly like the pain on the right side before operation. Left nephropexy was done, followed by complete and permanent relief of the left-sided pain. The pyelograms (fig. 1 *B*) made long after the two operations showed completely normal pelves and disappearance of the pelvic dilatation.

Comparison of the before and after pyelograms (fig. 1) show beautifully the anatomic accomplishment of operation. This is accompanied by complete symptomatic relief. The dilatation originally present appeared to be insignificant but its disappearance the result of operation suggests that actually it was significant.

On June 1, 1940, more than ten years after operation, the patient reported continuing complete relief. There seemed to be no warrant to make another check-up pyelogram at that time.

CASE 2.—A woman aged 21 had had periodic bilateral backache and attacks of severe pain in the right flank and right lower quadrant of the abdomen for seven years. The right and left pyelograms (fig. 2 *a*) showed the typical features of horseshoe kidney and slight pelvic dilatation.

6. Donohue, P. F.: J. Urol. **27**: 59-72 (Jan.) 1932.

Oct. 15, 1931, division of the isthmus and right nephropexy were made with immediate and permanent relief of the right-sided pain. During convalescence the patient began to have pain on the left side exactly like that on the right side before operation. Left nephropexy, December 8, was followed by complete and permanent relief of the left-sided pain.

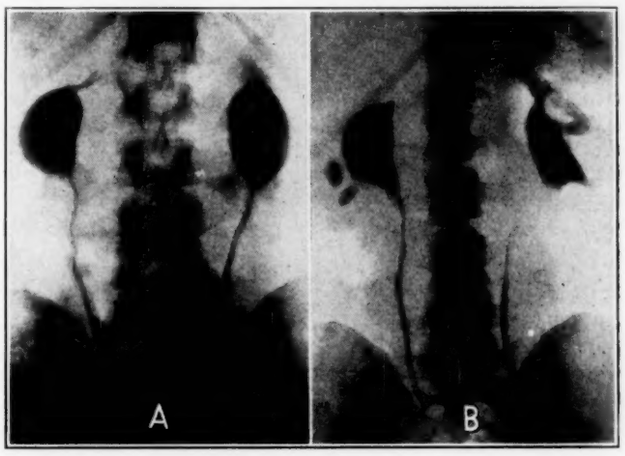


Fig. 5 (case 5).—*A*, preoperative bilateral pyelo-ureterogram; *B*, postoperative right and left pyelo-ureterograms.

Two years after operation a bilateral pyelogram (fig. 2 *B*) showed restoration to normal. Comparison of the before and after pyelograms (fig. 2) shows clearly what the operation accomplished.

On June 1, 1940, nine years after operation, the patient reported continuing complete relief. There seemed to be no warrant to make another check-up pyelogram at that time.

CASE 3.—A woman aged 25 had periodic pain in the right flank and right side of the abdomen for several years. Pyelograms (fig. 3 *A*) showed the typical features of horseshoe kidney with slight dilatation of each pelvis. Resection of the isthmus and right nephropexy were done in July 1933, followed by complete and permanent relief of the right sided pain.

Within a year the patient began to have pain on the left side exactly like that present on the right side before operation. Left nephropexy in January 1935 was followed by complete and permanent relief of the left-sided pain.

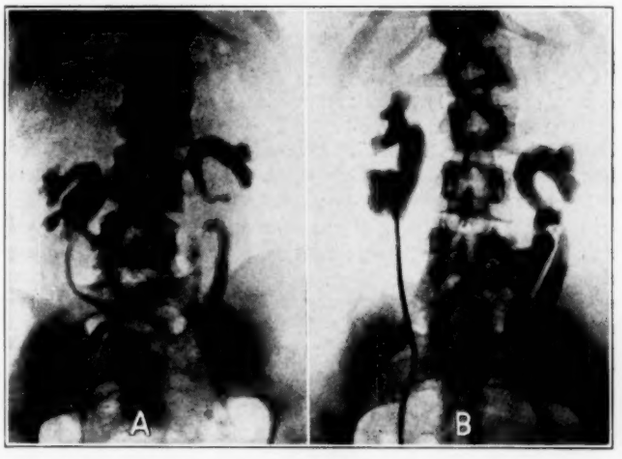


Fig. 6 (case 6).—*A*, preoperative bilateral pyelo-ureterogram; *B*, post operative bilateral pyelo-ureterogram.

Excretion urograms (fig. 3 *B*) made in April 1938, five years after the first operation, showed restoration to near normal. Comparison of the before and after pyelograms (fig. 3) shows well the anatomic accomplishment of the operation.

CASE 4.—This was the only case of failure. A man aged 38 had severe pain in the left flank, mild pain in the right flank and abdominal pain for several years. There was a stone in

the left kidney (fig. 4 *A*) and with it bilateral hydronephrosis (fig. 4 *B*) and deformity typical of horseshoe kidney. In June 1934 left pelviolithotomy, division of the isthmus and left nephropexy were done.

Later it was discovered the stone had been incompletely removed. Although the position of the kidney had been restored to near normal and the pelvic dilatation was slightly decreased (fig. 4 *C*) the infection persisted and secondary nephrectomy was done eight months later.

CASE 5.—A woman aged 30 had had frequent severe pain in the right flank and right side of the abdomen for five years and occasional mild pain in the left flank and left side of the abdomen. The bilateral pyelogram (fig. 5 *A*) showed the typical features of horseshoe kidney and bilateral hydronephrosis. In September 1934 division of the isthmus and right nephropexy were performed followed by gradual but finally complete relief of pain on the right side.

A year or so later the originally mild pain in the left flank and abdomen greatly increased. Left nephropexy in July 1938 was followed by complete and permanent relief. Relief of subjective symptoms has been complete and permanent. The most recent check-up pyelogram (fig. 5 *B*) was made June 5, 1940, five and one-half years after the first operation and two years after the second operation. A comparison of this with the original pyelogram (fig. 5) shows what was accomplished by the operation.

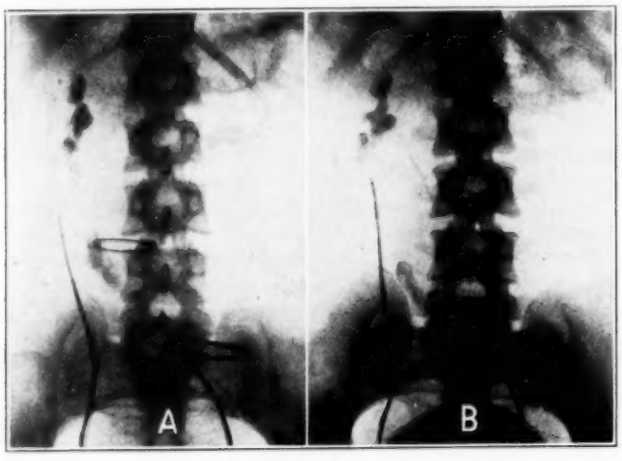


Fig. 7 (case 7).—*A*, preoperative bilateral pyelo-ureterogram; *B*, postoperative bilateral pyelo-ureterogram.

CASE 6.—A girl aged 19 years at first had attacks of severe pain in the right lower quadrant of the abdomen. Later there was constant bilateral lumbar pain. The pyelogram (fig. 6 *A*) showed the typical deformity of horseshoe kidney and grade 1 dilatation of each pelvis. On the left side there was duplication of the pelvis and upper ureter.

In July 1937 division of the isthmus and right nephropexy were performed. Following operation there were two attacks of acute pyelonephritis. Apart from these there has been complete and permanent relief of the right lower quadrant pain and of bilateral lumbar pain. The most recent check-up pyelogram (fig. 6 *B*) was made June 6, 1940, three years after operation. It showed normal position of the right pelvis but no decrease of dilatation and no change in position of the left pelvis.

A comparison of this recent pyelogram with the original preoperative pyelogram (fig. 6) shows what was accomplished by operation.

CASE 7.—This was a case of unilateral fused kidney and was originally reported in the February 1930 issue of *International Abstracts of Surgery*.[7]

A girl aged 18 complained of left-sided abdominal pain for three years, at times very severe. A mass was palpable in the right lower quadrant of the abdomen. The pyelogram (fig. 7 *A*) showed the typical features of unilateral fused kidney with crossed ectopia of the left and lower segment.

For relief of the left-sided pain, two operations were contemplated. The pain appeared to have its origin in the left half of the fused kidney. Preliminary to any surgical attack on the "crossed-ectopic" left half of the fused kidney it seemed wise first to divide the isthmus and fix in normal position the separated right kidney. With the right half of the fused kidney thus restored to normal position and normal function, it would then be possible safely to perform a left nephrectomy if later operation on the left side disclosed vascular attachments or other technical difficulties making impossible a conservative procedure.

In June 1937, through a right flank incision with extraperitoneal approach to the kidney, division of the isthmus and right nephropexy were done. Through this incision it was possible to displace the separated left kidney across the midline, though restoration of the left kidney to a completely normal position of course was not possible with this exposure.

The result to date, three years after operation, is excellent, there being complete relief of the left-sided pain complained of before operation. Since operation the patient has gone through an uneventful pregnancy terminated by normal delivery. In view of all this, no indication is found for doing the contemplated second operation on the left side.

The most recent check-up pyelogram (fig. 7 *B*) was made June 5, 1940, three years after operation. It gives very poor outlining of the lower or left pelvis but sufficient to show that its position is somewhat improved. The right pelvis is well up in normal position. A comparison of this with the pyelogram made before operation shows what was accomplished (fig. 7).

COMMENT

In all of these cases a lumbar incision and extraperitoneal approach to the kidney were employed. In all cases excellent exposure was secured: the procedure was carried out with facility and no formidable difficulty was encountered. In all cases relatively smooth convalescence followed the surgical procedure, and there was no mortality.

Items of interest in the occurrence and management of these cases are the following:

Six of the seven patients were women, all of whom were in the second or third decade. One patient was a man aged 38.

In all cases the chief complaint was pain and in most instances its character was fairly typical of renal origin. In all the cases obstruction and varying degrees of pelvic dilatation were demonstrated and in some there were varying degrees of upper tract infection and pyuria. In two of the cases the degree of pelvic dilatation amounted to outspoken hydronephrosis and one of these was complicated by stone.

In all cases operation was undertaken with relief of pain its chief objective. In all save one case (case 4) this object has been fully attained, with complete relief of painful symptoms. The one case of failure was due to faulty management, failure to remove a stone completely.

It should be noted that, in three cases (1, 2 and 3) of unilateral pain, division of the isthmus and relief of pain on the side of operation was followed in different periods by development of identical pain on the opposite side and that in these three cases correction of the abnormal position of the opposite half of the horseshoe kidney gave complete relief of the newly developed pain on the opposite side. In another case (case 5) originally mild pain on the opposite side gradually increased and a year and a half after the first operation was com-

7. Foley, F. E. B., and Wilmer, H. A.: Internat. Abstr. Surg. **70**: 155-170, 1940, in Surg., Gynec. & Obst., February 1940.

pletely relieved by nephropexy on the second side. In one case of bilateral pain (case 6) division of the isthmus and nephropexy on only one side gave relief of pain on both sides. In one case of unilateral fused kidney (case 7) left-sided pain was relieved by symphysiotomy and right nephropexy.

These seven cases make by far the largest individual experience thus far reported—in fact they represent almost a third of the total experience. In all save one case the eventual end result has been excellent ten years after operation in the earliest case, three years after operation in the most recent case.

The reports in the literature state the eventual end result in only three cases: excellent fourteen years, ten years and eight years after operation. In the case of Judd, Braasch and Scholl the result was excellent eighteen years after operation. In the remaining fifteen cases reported in the literature only the immediate result up to a few months after operation is stated, but in all it was excellent.

My own experience indicates that an immediately favorable result will prove to be a permanently favorable result if the case is followed long enough to bring the proof. At least among my seven cases there was only one eventual poor result (case 4) and this was due to mismanagement—the failure to remove a calculus completely. This personal experience, indicating that an immediately favorable result will be permanent, increases the significance of the early favorable results reported in the literature.

TABLE 2.—*Results of Symphysiotomy With or Without Nephropexy*

Cases reported in literature	19	
Cases, personal	7	
Cases, total	26	
Postoperative deaths	1	3½%
Poor results	1	3½%
Excellent or good results—early	14	54%
Excellent or good results—permanent	10	38%
Excellent or good results—total	24	92%
	26	

SUMMARY AND CONCLUSIONS

The eighteen cases reported in the literature, the case of Judd, Braasch and Scholl followed by personal communication and my seven cases here reported are summarized in table 2 and the results may be stated as follows:

There was a total of twenty-six cases.

There was one postoperative death.

There was one poor result, which was due to mismanagement.

There were twenty-four good results. Of these, fourteen were reported as early results and ten were reported as permanent results.

The material presented warrants the conclusions that:

1. The anomaly horseshoe kidney not accompanied by any significant pathologic change may be productive of painful and other symptoms.

2. The symptoms caused by the anomaly horseshoe kidney can be relieved and normal anatomic relations can be restored by division of the renal isthmus and nephropexy on one or both sides.

350 St. Peter Street.

ACUTE ASCENDING PARALYSIS

CLINICAL AND PATHOLOGIC REPORT ON CASES WITH FATAL TERMINATION

RUSSELL N. DeJONG, M.D.
ANN ARBOR, MICH.

In 1859 Octave Landry[1] described a case of acute ascending paralysis in which there were no changes in sensation, muscular atrophy or disturbances of the sphincters, and no abnormalities were observed in the postmortem examination. Cases of ascending paralysis in which the clinical course resembled the one described by Landry have been called Landry's paralysis by many observers, and a definite clinical syndrome has been described. A previously healthy individual, after suffering from mild prodromal symptoms such as malaise, paresthesias in the lower extremities, anorexia, constipation and occasionally slight fever, develops a sudden flaccid paralysis of the lower extremities which rapidly ascends, involving next the abdominal muscles, the intercostals, the upper extremities and in fatal cases the muscles supplied by the bulbar nerves. Cases of descending paralysis have also been described, but these occur less frequently. The process may result in death within a few days or weeks, or if improvement does take place there may be complete recovery, the function returning first in the muscles last affected.

An infectious or toxic etiology has usually been ascribed to the condition, and enlargement of the spleen, hyperplasia of the lymph nodes, albuminuria and nephritis have been observed in some cases.[2] Among the infectious diseases that have been complicated by an ascending paralysis are syphilis, tuberculosis, diphtheria, influenza, typhoid, measles, mumps, malaria, pertussis, encephalitis, rabies, Rocky Mountain fever, smallpox, vaccinia, pneumonia, anthrax, varicella, gonorrhea and herpes. Rabies vaccine, diphtheria and tetanus antitoxin, alcohol, lead, arsenic and hematoporphyria have been reported as toxic etiologies. In a few instances organisms have been isolated from the cerebrospinal fluid or the spinal cord,[3] but bacteriologic studies have given no consistent or conclusive results. A recent translator of Landry's original description and other authors believe that vitamin deficiency should be considered as an important etiologic factor,[4] but this hypothesis remains to be proved. The term Landry's paralysis has also been erroneously applied to cases of poliomyelitis, transverse myelitis, myelomalacia[5] and other varieties of myelitis of known etiology characterized by an ascending type of paralysis, but these conditions should obviously be differentiated from the true Landry type.

From the Department of Neurology, University of Michigan Medical School and University Hospital.

Read before the Section on Nervous and Mental Diseases at the Ninety-First Annual Session of the American Medical Association, New York, June 12, 1940.

1. Landry, Octave: Note sur la paralysie ascendante aiguë, Gaz. hebd. de méd. **6:** 472 (July 9), 486 (Aug. 5) 1859.

2. Wechsler, I. S.: A Textbook of Clinical Neurology, ed. 3, Philadelphia, W. B. Saunders Company, 1935, p. 125.

3. Boinet: Un cas de paralysie de Landry, Gaz. d. hôp. **72:** 458 (May 2) 1899. Bradford, J. R.; Bashford, E. F., and Wilson, J. A.: Acute Infective Polyneuritis, Quart. J. Med. **12:** 88 (Oct.) 1918. Courmont, P.: Syndrome de Landry par lésions exclusives des cornes antérieures, Arch. de neurol. **8:** 353 (Nov.) 1899. Leschke, E.: Ueber der Erreger der Landry'schen Paralyse, Berl. klin. Wchnschr. **51:** 783 (April 27) 1914.

4. Brown, M. R.: Etiologic Study of Landry's Original Case of Acute Ascending Paralysis, Arch. Neurol. & Psychiat. **40:** 800 (Oct.) 1938. Shattuck, G. C.: "Landry's Paralysis" in Relation to Vitamin B Deficiency, Internat. Clin. **1:** 25 (Sept.) 1938.

5. Low, A. A., Acute Ascending Myelomalacia, Arch. Neurol. & Psychiat. **21:** 594 (March) 1929.

The pathologic observations in cases classified as Landry's paralysis have been varied and inconsistent. The earlier writers believed that pathologic changes were absent; this opinion may have arisen as the result of the lack of technical facilities at the time, although cases are still being reported in which no lesions are found. Oppenheim [6] stated that the postmortem appearances were indefinite and contradictory; in many cases the examination was negative, in some there were disseminated foci of inflammation and exudation with capillary hemorrhages and swelling of the axis cylinders, and others showed inflammation of the anterior horns or a combination of a neuritis and a myelitis. He felt that in most cases the conditions resembled those seen in polyneuritis without being identical with it. Cadwalader [7] described hyperemia and edema of the gray matter of the spinal cord with varying changes in the anterior horn cells but stated that there appears to be no certain method of determining whether the disease process originates in the nerve fibers, in the spinal cord, or in both. At the present, however, most authors agree that purely degenerative changes take place either in the anterior horn cells or in the peripheral nerves, but there are no evidences of inflammation or infiltration, no glial proliferation, and no degenerative changes in the white matter of the spinal cord.[8]

Many authors have questioned the use of the term Landry's paralysis and the consideration of the condition as a nosologic entity.[9] As early as 1891 Eichberg stated that the name was unscientific and should be dropped. Much misunderstanding has resulted, however, from the fact that many dissimilar conditions have been classified as Landry's paralysis. Eichberg's own case obviously did not belong to the Landry group, as it showed an acute inflammatory reaction in the anterior horn cells, the perivascular spaces and the meninges. Other authors have added to the confusion by using the term Landry's paralysis for cases of poliomyelitis and polyneuritis in which the paralysis was of an ascending nature. Grinker,[10] for example, states that poliomyelitis is the most common cause of Landry's paralysis and that diphtheritic polyneuritis is the next in frequency. Cobb and Coggeshall [11] say that most cases diagnosed as Landry's paralysis are fulminating examples of ordinary infantile paralysis. According to Osler [12] the differentiation between multiple neuritis and Landry's paralysis is often difficult, and it may be impossible in cases with sensory changes. Taylor and McDonald [13] considered ascending paralysis as a transitional form between conditions in which the pathologic changes are predominantly in the spinal cord and a complicated group of polyneuritides. Collier [14] believes that the separation of Landry's paralysis and polyneuritis is artificial and that Landry's paralysis is a polyneuritis with associated spinal cord involvement; he [15] even went so far as to say, in his Morrison Lectures before the Royal College of Physicians of Edinburgh in 1932, that Landry's paralysis is one of the most characteristic of all forms of peripheral neuritis—a destruction of function, rapidly advancing, spreading by tissue continuity, without discoverable histologic changes and, when not fatal, rapidly and completely recovering, and that every grade of transitional form between the rapidly spreading Landry's paralysis and the slowly advancing types of peripheral neuritis may be encountered.

Attempts at classification and differentiation of the various types of ascending paralysis have been of some value in understanding the group as a whole but have not entirely clarified the subject. Some authors [16] have differentiated the poliomyelitic and polyneuritic varieties from those showing little or no pathologic change. Pette and Környey [17] separated cases with purely degenerative changes, apparently on a toxic basis, from those showing outspoken signs of inflammation. They subdivided instances of Landry's paralysis showing inflammatory changes into those in which the evidences of inflammation were predominantly central, or cases of atypical poliomyelitis, and those in which the pathologic changes were predominantly peripheral. Two instances of the latter group were described by them and classified as cases of Landry's paralysis, but both showed sensory changes and loss of sphincter control, thus making the clinical diagnosis doubtful, and in addition the postmortem examination revealed lymphocytic and plasma cell infiltrations in the ganglions, the nerve roots and the meninges. Juba [18] described a similar case in which there were degenerative changes associated with infiltrations in the spinal ganglions, but he spoke of this as a polyneuroganglioradiculitis, which is obviously a better term.

Certain authors believe, however, with Gordinier [19] that ascending paralysis is a specific type of myelitis of unknown etiology which can be differentiated, both clinically and pathologically, from poliomyelitis and polyneuritis, even in complicated cases. The former can, as a rule, be excluded by its epidemiologic features, clinical signs, characteristic cerebrospinal fluid changes and definite patho-anatomic picture. In polyneuritis there is simultaneous involvement of both sensory and motor nerves, the process being manifest in various portions of the body but failing to follow the distribution usually seen in acute ascending paralysis. Even

6. Oppenheim, Hermann: Lehrbuch der Nervenkrankheiten, ed. 7, Berlin, S. Karger, 1923, pp. 832-840.

7. Cadwalader, W. B.: Diseases of the Spinal Cord, Baltimore, Williams & Wilkins Company, 1932, pp. 139-142.

8. Büttner, W.: Zur Klinik, pathologischen Anatomie und Nosologie der aufsteigenden Lähmung (sogen. Landryschen Paralyse), Monatschr. f. Psychiat. u. Neurol. **75**: 279 (April) 1930. Courville, C. B.: Pathology of the Nervous System, Mountain View, Calif., Pacific Press Publishing Association, 1937, p. 179. Freeman, Walter: Neuropathology, Philadelphia, W. B. Saunders Company, 1933, p. 168. Gärtner, W.: Poly-Neuro-Radiculitis ascendens (Landryscher Symptomenkomplex), Deutsche Ztschr. f. Nervenh. **123**: 18, 1931. Pawljutschenko, E. M.: Zur Klinik und pathologischen Anatomie der "akuten aufsteigenden Landryschen Paralyse," Arch. f. Psychiat. **89**: 570, 1930. Collier.[14]

9. Eichberg, J.: A Case of Acute Ascending Paralysis—Rapidly Fatal Issue, M. Rec. **39**: 226 (Feb. 21) 1891. Taylor, E. W., and Clark, J. E.: Landry's Paralysis: Remarks on Classification, J. Nerv. & Ment. Dis. **27**: 177 (April) 1900.

10. Grinker Roy R.: Neurology, Springfield, Ill., and Baltimore, Charles C. Thomas, 1934, p. 221.

11. Cobb, Stanley, and Coggeshall, H. C.: Neuritis, J. A. M. A. **103**: 1608 (Nov. 24) 1934.

12. Osler, William: The Principles and Practice of Medicine, New York, D. Appleton & Co., 1892, p. 836.

13. Taylor, E. W., and McDonald, C. A.: The Syndrome of Polyneuritis with Facial Diplegia, Tr. Am. Neurol. A. **57**: 210, 1931.

14. Collier, James: Landry's Paralysis, in Christian, H. A.: Oxford Medicine, New York, Oxford University Press, 1936, vol. 6, pt. 1, p. 419.

15. Collier, James: Peripheral Neuritis, Edinburgh M. J. **39**: 601 (Oct.) 1932.

16. Marie, P., and Tretiakoff, C.: Etude anatomo-pathologique de trois cas de maladie de Landry a forme médullaire, Rev. neurol. **37**: 777 (July-Aug.) 1921. Goldby, Frank: Landry's Paralysis: A Clinical and Pathological Study, J. Neurol. & Psychopath. **11**: 1 (July) 1930. Calleweart, P.: Deux observations anatomocliniques de maladie de Landry, J. belge de neurol. et de psychiat. **36**: 368 (June) 1936.

17. Pette, H., and Környey, S.: Zur Histologie und Pathogenese der akutentzündlichen Formen der Landryschen Paralyse, Ztschr. f. d. ges. Neurol. u. Psychiat. **128**: 390, 1930.

18. Juba, A.: Ueber einen perakut verlaufenen Fall von Polyneuroganglioradiculitis ascendens, Deutsche Ztschr. f. Nervenh. **142**: 265, 1937.

19. Gordinier, H. C.: Poliomyelitis versus Landry's Paralysis, Ann. Int. Med. **3**: 892 (March) 1930.

in conditions such as "infectious neuronitis" (Foster Kennedy; Gilpin, Moersh and Kernohan,[20] and others) and in the cases of ascending paralysis in troops described by Casamajor,[21] a clinical and pathologic differentiation can usually be reached. The same is true of the cases of polyneuritis with albuminocytologic dissociation described by Guillain and Barré.[22]

In an effort to evaluate these varying points of view and to come to some conclusions as to the justification of the use of the terms ascending paralysis or Landry's paralysis, some cases that have recently been studied both clinically and pathologically in the University Hospital have been reviewed.

REPORT OF CASES

CASE 1.—M. K., a painter aged 65, had noticed shooting pains in the feet for several months. Three weeks before admission he had diarrhea and a slight head cold and two weeks later had suddenly become nauseated, vomited, and noted cramping pains in the lower part of the abdomen. Following this he had weakness and later an ascending paralysis, first involving the feet, then the thighs, trunk and upper extremities. There was tingling of the hands and feet but no definite loss of sensation, and there was no disturbance of bowel or bladder control. Two days before admission he developed hoarseness, dysphagia, and weakness of the neck muscles, and shortly after this difficulty in breathing.

On admission the patient was dyspneic and cyanotic. Respirations were intercostal in type. Speech was reduced to a whisper and swallowing was difficult. There was limitation of lateral rotation of the eyeballs to each side; the ocular fundi were normal, as was the reaction of the pupils. There was weakness of the muscles of facial expression on both sides, and

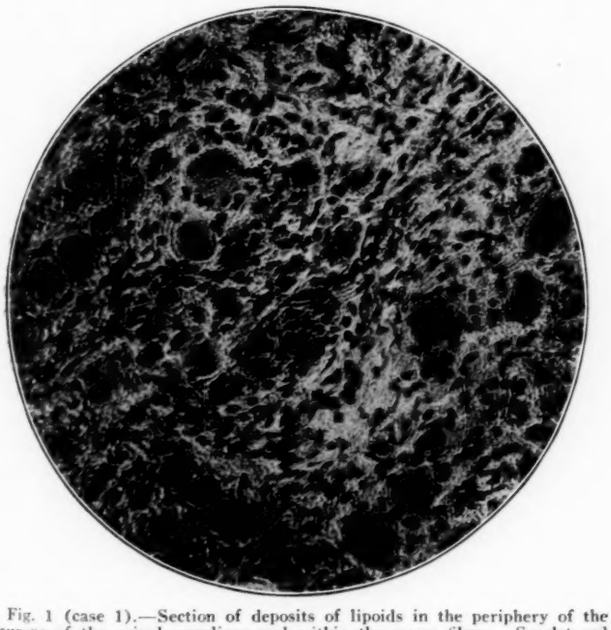


Fig. 1 (case 1).—Section of deposits of lipoids in the periphery of the neurons of the spinal ganglions and within the nerve fibers. Scarlet red stain; Zeiss objective 40 ×; ocular F 2.

the soft palate could not be elevated. The tongue could not be protruded beyond the lips, but there was no atrophy or tremor. There was bilateral weakness of the sternocleidomastoid and trapezius muscles. The patient was unable to move his extremities. The tendon and abdominal reflexes were absent. There was no response following plantar stimulation. The sensory examination was unsatisfactory but no definite disturbance in sensation was elicited.

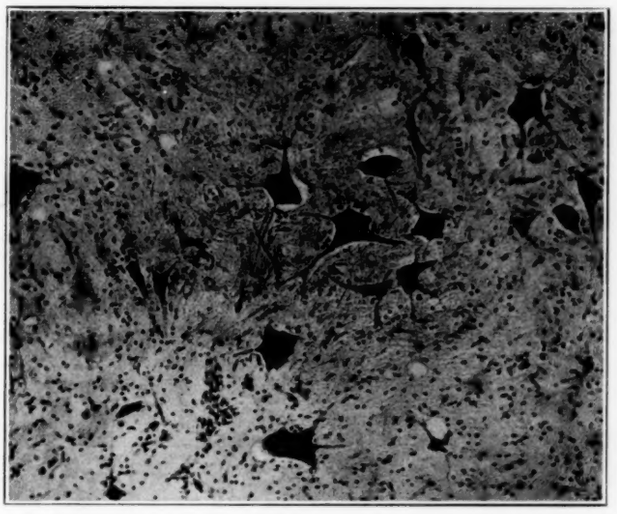


Fig. 2 (case 1).—Section of anterior horn cells showing shrinkage and pyknosis. Nissl stain; Zeiss objective 40 ×; ocular F 2.

Because of the marked difficulty in breathing the patient was placed in a respirator on admission to the hospital, and as a result further examinations including those of the cerebrospinal fluid could not be carried out. There was a gradual failure of respiration and circulation, and death occurred in forty-eight hours.

The postmortem examination revealed an acute purulent bronchitis and bronchopneumonia with atelectasis, emphysema and pulmonary congestion. The brain and spinal cord were edematous and hyperemic and the meninges were congested. There were many small hemorrhages into the meninges and the gray matter of the cord. The predominant microscopic pathologic changes were noted in the nerve roots and the spinal ganglions. There were large deposits of lipoids in the periphery of the neurons and within the nerve fibers, as demonstrated both by scarlet red and by osmic acid stains (fig. 1). The structure of the ganglions and nerve fibers was otherwise unchanged, the myelin was not appreciably broken down, and there was no evidence of inflammation. Nissl stains of the spinal cord showed shrinkage, pyknosis and varying degrees of chromatolysis of the anterior horn cells (fig. 2), and scarlet red and osmic acid stains showed lipoids within the neurons. There were many small hemorrhagic areas in the gray matter, some of which were surrounded by minute areas of necrosis. There were no evidences of infiltration, inflammation or exudation in the nerves or the spinal cord, and there was no destruction of the myelin sheaths. No definite pathologic changes were demonstrable in the nuclear area of the pons or medulla.

CASE 2.—Mrs. B. S., a white woman aged 48 whose past medical history was without significance, had been well until two weeks before admission to the hospital, at which time she had an attack of respiratory difficulty diagnosed as asthma and relieved by oral and hypodermic medication. One week later she noticed heaviness and progressive weakness of the feet, which ascended to involve the legs and later the arms and hands. There were paresthesias in the hands and feet, but there was no definite loss of sensation.

At the time of admission the patient was dyspneic and moderately cyanotic. Moist rales were heard throughout the lungs and there was an area of dulness at the base of the left lung. There was no disturbance of superficial sensation or of sense of position; vibratory sense was slightly diminished at the ankles, but deep pain sense was increased in the calf muscles and achilles tendons. The pupils reacted normally to light and in accommodation. The extra-ocular movements were

20. Kennedy, Foster: Infective Neuronitis, Arch. Neurol. & Psychiat. **2**: 621 (Dec.) 1919. Gilpin, S. F.; Moersch, F. P., and Kernohan, J. W.: Polyneuritis: A Clinical and Pathologic Study of a Special Group of Cases Frequently Referred to as Instances of Neuronitis, Arch. Neurol. & Psychiat. **35**: 937 (May) 1936.

21. Casamajor, Louis: Acute Ascending Paralysis among Troops, Arch. Neurol. & Psychiat. **2**: 605 (Dec.) 1919.

22. Guillain, G.; Barré, J. A., and Strohl, A.: Sur un syndrome de radiculo-névrite avec hyperalbuminose du liquide céphalo-rachidien sans réaction cellulaire, Bull. et mém. Soc. méd. d. hôp. de Paris **40**: 1462 (Oct. 13) 1916.

normal. There was a slight but definite weakness of the muscles supplied by the left facial nerve. Articulation was normal. The sternocleidomastoid and trapezius muscles contracted normally and the tongue protruded in the midline. Aside from shrugging of the shoulders the patient was unable to carry out any movement of the upper or lower extremities. There was no atrophy, and no fibrillations were seen. All tendon and cutaneous reflexes were absent. There were no pyramidal tract signs. The urinalysis, blood count, and blood Kahn test gave negative results. The spinal fluid pressure was 150 mm. of water, with no block, and the fluid contained one lymphocyte per cubic millimeter; the Pandy and Nonne-Apelt tests were strongly positive, the total protein content was 111 mg. per hundred cubic centimeters, the Kahn reaction was negative, the colloidal gold curve was 0011100000, and the mastic curve was 122100. Examination of the urine, hair and nails for lead and arsenic was carried out with negative results.

The paralysis of the extremities continued unabated, and two days after admission the patient noted difficulty in swallowing and talking with progressive respiratory distress. Pneumonia developed and death occurred two weeks after admission.

The postmortem examination showed bronchopneumonia in the lower lobe of the left lung and atelectasis in the lower lobe of the right. Gross examination of the brain revealed pronounced hyperemia. In the spinal cord the predominant congestion was in the anterior horns, the cells of which showed marked swelling with displacement of the nuclei. The tigroid substance was broken down; in some cells it was evenly distributed throughout and dustlike in appearance, while other cells stained a deep pinkish blue with thionin and showed no details. Many of the swollen cells contained large vacuoles, and some with three or more exhibited a honeycombed appearance (fig. 3). Scarlet red and Marchi stains showed accumulations of lipoids within the neurons. The vessels of the cord were congested and engorged but there was no evidence of infiltration or exudation and no degeneration of the myelin sheaths. The motor nuclei within the medulla showed changes similar to those present in the anterior horn cells. There was no inflammatory reaction in the ganglions and no definite evidence of any pathologic process in the peripheral nerves.

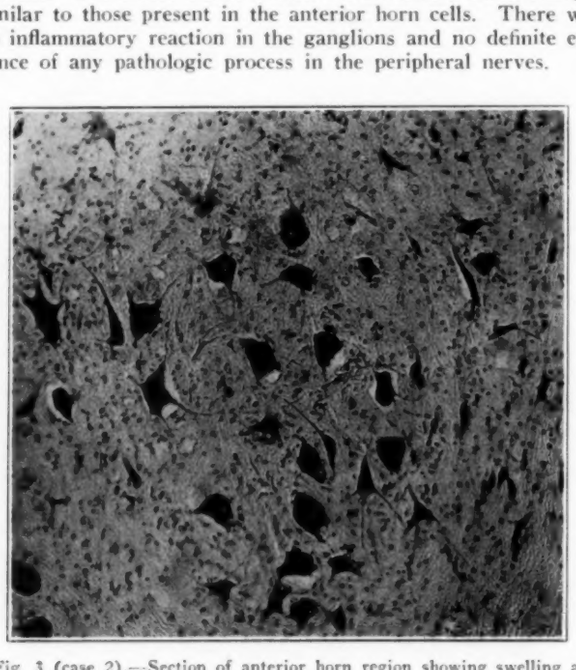


Fig. 3 (case 2).—Section of anterior horn region showing swelling and vacuolization of neurons. Nissl stain; Zeiss objective 40 ×; ocular F 2.

CASE 3.—M. P., a girl aged 18 months, developed what appeared to be pain in the legs and later in the arms, followed by a complete paralysis of the lower and a partial paralysis of the upper extremities. There was a brief elevation of temperature at the time of the onset of the symptoms. Six weeks later respiratory difficulty appeared and the temperature again became elevated.

At the time of admission to the hospital the patient was dyspneic and cyanotic. The respirations were 30 per minute, the pulse rate was 130 and the rectal temperature was 101 F. There was dulness with bronchial breathing over the base of both lungs. The pupils reacted normally and there was no apparent difficulty in talking or swallowing. There was a flaccid paralysis of the upper and lower extremities. The triceps reflexes were diminished, and the biceps, patellar and achilles reflexes were absent. The abdominal reflexes were not obtained. There was no Babinski sign. Superficial and deep pain sensations were apparently normal. There was no demonstrable muscle tenderness and there were no signs of meningeal irritation. The urinalysis and the Kahn tests on the blood gave negative results. Blood count showed 13,050 leukocytes per cubic millimeter, 79 per cent of which were polymorphonuclear cells. A spinal puncture was not performed.

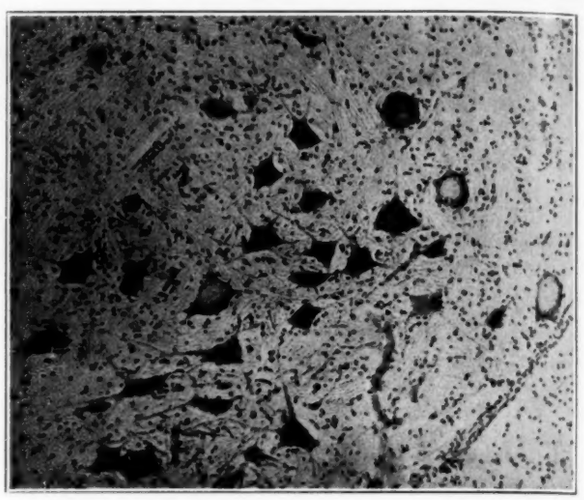


Fig. 4 (case 3).—Section of anterior horn region showing outspoken primary irritation of the neurons with chromatolysis and swelling. Nissl stain; Zeiss objective 40 ×; ocular F 2.

The child was placed in an oxygen tent but her respiratory difficulty increased and she became unable to swallow. Death occurred twenty-four hours after admission.

The postmortem examination showed a severe bilateral, confluent, purulent, lobular pneumonia. There were moderate congestion and edema of the brain, meninges and spinal cord but no other gross pathologic abnormalities. Microscopic examination showed pronounced changes in the anterior horn cells, especially in the lumbar and sacral segments. The cells were greatly swollen and many were vacuolated. The tigroid substance was disintegrated and broken down into fine dustlike particles which stained a pinkish blue with thionin. The nuclei were either shrunken and pushed to the periphery of the cells or were completely destroyed (fig. 4). In other segments, especially those of the thoracic cord, there were fewer swollen cells but many which stained a deep blue so that few details could be made out, and some which were reduced to indistinctly outlined bodies filled with disintegrated tigroid material. In certain sections the neurons in the anterior horns were greatly reduced in number and those which remained were small and shrunken. There were no signs of inflammation or glial proliferation and there was no degeneration of myelin. The peripheral nerves were normal. There were no demonstrable changes in the medulla.

CONCLUSIONS

These are instances of acute ascending paralysis of unknown etiology. The pathologic changes were not identical, but in all there were evidences of a degenerative process involving the motor nuclei or the peripheral nerves or both. There were no signs of inflammation, such as cellular infiltration or glial proliferation, and no degenerative changes in the white matter of the spinal cord. The predominant gross pathologic finding was hyperemia of the anterior horn region. The outstanding microscopic change, the degen-

eration of the neurons, assumed different forms. In case 1 it consisted of shrinkage and pyknosis, which may be considered as a primary phenomenon, but it was accompanied by degenerative changes in the nerve roots and the spinal ganglions. In case 2 there were swelling, chromatolysis, displacement and fragmentation of the nuclei, and vacuolization, which is assumed to indicate an axonal type of degeneration secondary to changes in the axis cylinders. Case 3 showed a pronounced axonal reaction in some segments with pyknosis and reduction in the number of the neurons in others. It can be assumed from these observations that the degenerative process is one that involves either the motor nuclei or the peripheral nerves or both and is therefore characterized by involvement of part or all of the final common pathway of the motor impulses. In spite of some variability in the changes they were purely degenerative in all cases, and to a certain extent each showed some evidence of both pyknosis and swelling. It is entirely possible that the syndrome is a transitional form between certain types of polyradiculoneuritis (Guillain-Barré syndrome) and varieties of myelitis and encephalitis.

The etiology of the process cannot be arrived at from this study. As there are no signs of inflammation and the changes in the nervous system are essentially degenerative in nature, it can probably be assumed that we are dealing with an acute toxic process affecting both the central and the peripheral nervous system.[23] A filtrable virus etiology has been suggested, but this has not yet been proved.[24]

Precedent has established the use of the terms Landry's paralysis and acute ascending paralysis. Diller[25] in 1902 stated: "The term Landry's paralysis cannot be dropped. It has been used too long to be erased from our nomenclature." If these terms are to be used, however, they should not be interpreted as signifying a definite nosologic entity due to a single etiology. The terms should be used only in those cases in which the clinical syndrome is similar to that described by Landry and no definite etiology such as poliomyelitis or some specific toxin or infection is suspected. When the foregoing terms are used they should be considered as descriptive of the mode of onset and progression of the condition[2] rather than as a final diagnosis. Cases in which the etiology is known but the syndrome closely resembles that seen in acute ascending paralysis may be spoken of as cases of Landry's syndrome.

23. Brussilowski, L.: Zur Lehre von der akuten aufsteigenden Landryschen Paralyse, Ztschr. f. d. ges. Neurol. u. Psychiat. **111:** 515, 1927. Grünewald, E. A.: Studien zur Pathogenese der Landryschen Paralyse, J. f. Psychol. u. Neurol. **29:** 403, 1923. Willis, F. E. S., and Jewell, J. W. F.: A Case of Landry's Paralysis of Descending Type, Lancet **1:** 132 (Jan. 18) 1930.

24. Demme, H.: Zur Pathogenese der entzündlichen Form der Landryschen Paralyse, Deutsche Ztschr. f. Nervenh. **125:** 1, 1932. Cobb and Coggeshall.[11]

25. Diller, Theodore: A Study of Landry's Paralysis, with a Report of Three Nonfatal Cases, J. Nerv. & Ment. Dis. **29:** 577 (Oct.) 1902.

Normal Food Requirements.—Gillett has suggested that the family food budget be divided into fifths: one fifth for vegetables and fruits, one fifth or more for milk and cheese, one fifth or less for meat, fish and eggs, one fifth or more for bread and cereals and one fifth or less for sugars, fats and other groceries and food adjuncts. Whatever the level of food expenditure, at least as much should be spent for milk (including cream and cheese) as for meats, poultry and fish, and as much should be spent for fruits and vegetables as for meat, poultry and fish.—Smillie, Wilson G.: Public Health Administration in the United States, New York, Macmillan Company, 1940.

POLYRADICULONEURITIS (GUILLAIN-BARRÉ SYNDROME)

FOLLOWING THE USE OF SULFANILAMIDE AND FEVER THERAPY

PAUL H. GARVEY, M.D.
NATHANIEL JONES, M.D.
AND
STAFFORD L. WARREN, M.D.
ROCHESTER, N. Y.

During recent years two valuable therapeutic agents, sulfanilamide and fever therapy, have been added to the armamentarium in the treatment of disease. However, like other therapeutic measures, they may be accompanied or followed by undesirable effects in a certain percentage of cases. It is often difficult to decide, when two therapeutic agents are used concomitantly or consecutively, which agent is responsible for the favorable effect on the disease or, in some instances, even the undesirable complication.

Numerous toxic manifestations have been described following the use of sulfanilamide and its derivatives. Reports indicating a toxic action of sulfanilamide on the peripheral nervous system are few. Ornsteen and Furst[1] reported a case of peripheral neuritis which followed the ingestion of 130 Gm. of sulfanilamide. Janet[2] observed one case of multiple neuritis of the arm and thorax which lasted only three days. Waugh[3] recently reported a case of neuritis of the left anterior tibial nerve occurring in a patient with gonorrhea during treatment with sulfanilamide. This was the only case which he observed in 650 cases in which intensive sulfanilamide therapy was administered. A case of optic neuritis was reported by Bucy.[4] However, peripheral neuritis has been frequently reported following the use of disulfyl-sulfanilamide. Recently we have observed two cases of peripheral neuritis which developed in patients treated for staphylococcic infections with sulfamethylthiazole.

Certain evanescent symptoms referable to the nervous system may occur during fever treatment. In this clinic we have occasionally observed such symptoms as delirium, coma, convulsions, vomiting and localized muscular weakness. These symptoms have been attributed to dehydration, cerebral edema, anoxemia and in a few cases of syphilis probably actual vascular lesions in the central nervous system. These symptoms are found during or immediately following treatment.

During the past two years we have observed six cases in which a more extensive and rather definite, stereotyped syndrome developed from ten to sixteen days following fever treatments of fifteen hours at 41.5 C. (106.7 F.). Nothing similar had been noted following the treatment of approximately 1,100 fever cases since 1930, and the syndrome is so striking and temporarily disabling as to have been called to our attention before this, if it has occurred in our group of patients.

Read before the Section on Nervous and Mental Diseases at the Ninety-First Annual Session of the American Medical Association, New York, June 12, 1940.

From the Department of Medicine, Division of Neurology (Drs. Garvey and Jones) and the Department of Radiology (Dr. Warren) of the University of Rochester School of Medicine and Dentistry.

1. Ornsteen, A. M., and Furst, William: Peripheral Neuritis Due to Sulfanilamide, J. A. M. A. **111:** 2103-2104 (Dec. 3) 1938.

2. Janet, Jules: Protest Against Sale of Sulfanilamide over the Counter, Paris letter, J. A. M. A. **110:** 1501 (April 30) 1938.

3. Waugh, J. R.: Peripheral Neuritis During Administration of Sulfanilamide, Am. J. Syph., Gonor. & Ven. Dis. **23:** 745 (Nov.) 1939.

4. Bucy, Paul C.: Toxic Optic Neuritis Resulting from Sulfanilamide, J. A. M. A. **109:** 1007-1008 (Sept. 25) 1937.

The syndrome under discussion in many respects is similar to that described by Guillain, Barré and Strohl [5] and is generally known as the Guillain-Barré syndrome. They describe it as a syndrome characterized by motor disturbances, loss of tendon jerks with preservation of cutaneous reflexes, paresthesias with slight disturbances of objective sensitivity, tenderness on pressure of the muscles, little changes in the electrical reaction of nerve or muscles, and noteworthy hyperalbuminosis of the cerebrospinal fluid in the absence of cytologic reaction (albuminocytologic dissociation).

REPORT OF CASES

CASE 1.—B. S., a girl aged 17 years, was admitted to the Rochester Municipal Hospital on June 20, 1938, because of lower abdominal pain and a vaginal discharge of three months' duration. A diagnosis of gonorrheal cervicitis was made at a local hospital and she received 38 Gm. of sulfanilamide between April 6 and April 10, 1938. Cervical cultures for Neisseria gonorrhoeae were positive following the course of sulfanilamide, and she was referred to this hospital for fever therapy.

The patient was well developed and well nourished. Vital signs were normal. The general physical examination was negative, except for some erosion of the cervix and a thick purulent vaginal discharge. Neurologic examination was negative.

Examination of the blood revealed 5,100,000 red blood cells, hemoglobin content 85 per cent, white cells 12,000. The Kahn and Wassermann tests were negative. The nonprotein nitrogen was 27 mg. per hundred cubic centimeters, icterus index 6, blood chlorides (under oil) 626 mg. per hundred cubic centimeters. Cervical cultures revealed Neisseria gonorrhoeae with a thermal death time of twenty hours at 41.5 C.

After the routine preparation for fever therapy on June 24 she was given fifteen hours of fever at 41.5 C. with a vaginal heater at 43.5 in situ for eight hours. She tolerated the procedure well except for postfever nausea and vomiting (chloride deprivation). On the second day following fever she became clinically icteric and had an icterus index of 20. On June 26 she was given an infusion of 1,000 cc. of 5 per cent dextrose solution into both thighs. Following this her recovery was uneventful. Three successive cervical cultures were negative prior to her discharge from the hospital on July 1.

The patient returned to the clinic on July 5 complaining of pain and soreness of both thighs. The temperature and pulse were normal. Both thighs were tender, swollen and indurated. A diagnosis of thrombophlebitis was made. The swelling and tenderness promptly subsided with rest in bed and she was discharged four days later.

On August 13 she was admitted to the hospital because of difficulty in walking. This symptom had been first noticed following her last discharge from the hospital on July 9. Associated with the disturbance of gait, which frequently caused her to fall, she had sharp shooting pains which radiated down both lower extremities. There was no history of sphincter or sensory disturbance.

On examination the cranial nerves were normal. Neurologic survey of the upper extremities was negative. The abdominal reflexes were present. The lower extremities were weak. She was able to walk unassisted, but the gait was waddling and unsteady. The calf muscles were flabby and one observer noted fibrillary tremors in the thigh muscles. The knee jerks were normal and the achilles reflexes diminished. There was no sensory disturbance. The plantar reflex was flexion on both sides. There were no abnormal physical manifestations.

A lumbar puncture on August 16 yielded a clear, colorless fluid under pressure of 190 mm. of water. The Queckenstedt test was negative. The fluid contained 4 cells per cubic millimeter. Total protein was 170 mg. per hundred cubic centimeters. The Wassermann reaction and gold curve were negative. On September 10 the spinal fluid was normal except for a total protein content of 140 mg. per hundred cubic centimeters. The spinal fluid at the time of the last puncture on November 21 was normal. The total protein content was 45 mg. per hundred cubic centimeters. The examination of the patient in December 1939 revealed no abnormalities.

CASE 2.—M. P., a man aged 34, was admitted to Strong Memorial Hospital on Nov. 8, 1938, because of a persistent urethral discharge. In 1936 the patient contracted an anterior urethritis, which gradually cleared up with local treatments given over a period of nine months. Two months before admission, one week following exposure, he again noted a profuse urethral discharge. During October he received 63 Gm. of sulfanilamide, 50 cc. of azosulfamide intramuscularly, and seven five hour fever treatments at another institution, without any decrease in the amount of the urethral discharge. He was then referred to this hospital for generalized hyperthermia.

The patient was well developed. The physical examination was negative except for the profuse urethral discharge. There were no abnormal neurologic symptoms or signs.

Examination of the blood revealed a moderate normocytic anemia. The hemoglobin was 10.8 Gm., red blood cells 3,090,000 per cubic millimeter, white blood cells 9,000. Blood chemistry was within normal limits. The Wassermann and Kahn tests on the blood were negative. The gonorrhea complement fixation test was plus-minus. Gonococci were cultured from the first specimen of voided urine. The thermal death time for the strain isolated was in excess of twenty-three hours at 41.5 C.

On November 11 he was given fifteen hours of fever therapy at 41.5 C. He tolerated the procedure well and without any postfever reaction or change in the blood chemistry. Three successive urethral cultures were negative for Neisseria gonorrhoeae and he was discharged on November 15.

The patient returned to the hospital on December 4 complaining of weakness and stiffness of the legs. These symptoms began twelve days after the hyperthermia. Associated with the weakness there were mild paresthesias of the legs and hyperhidrosis of the feet. He had no symptoms referable to the cranial nerves, upper extremities or sphincters. The general physical examination showed no abnormalities of the cranial nerves or upper extremities. There was weakness of both legs, particularly the flexors of the thighs and dorsiflexors of the feet. The gait was rather characteristic of that seen in progressive muscular dystrophy. He had difficulty in climbing stairs and he was unable to stand on his toes. The knee reflexes were present but diminished. The left achilles reflex was not definitely elicited and the right was greatly diminished. Tactile and thermal sensations were diminished over the feet and lower half of the legs. Vibration sensation was diminished over the malleoli but postural sensation of the toes was normal. There was excessive perspiration of the feet. The calf muscles were tender to palpation. A lumbar puncture yielded a clear, colorless spinal fluid under pressure of 110 mm. of water. The Queckenstedt test was normal. The fluid contained 4 cells per cubic millimeter and the total protein was 160 mg. per hundred cubic centimeters. Blood and spinal fluid Wassermann tests were negative. The colloidal gold curve was 0000121000. The patient was discharged from the hospital on December 6.

The patient returned to the hospital on December 22 and reported considerable improvement in gait and muscle power. The neurologic signs remained unchanged. A second lumbar puncture yielded a normal spinal fluid except for a total protein content of 110 mg. per hundred cubic centimeters. Further follow-up on this case was impossible, since the patient left the country at this time.

CASE 3.—F. S., a youth aged 18, was admitted to the Rochester Municipal Hospital on Feb. 11, 1939, because of sore throat, rash and a penile lesion. Six weeks before admission he was exposed to syphilis and two weeks following this exposure he developed a hard, painless, ulcerative lesion of the glans penis. The penile lesion began to heal after a period of about three weeks and at about this time he developed a macular eruption over the trunk and upper extremities. Three days before admission he developed a severe sore throat and pain in the

5. Guillain, Georges; Barré, J. A., and Strohl, A.: Sur un syndrome de radiculoneurite avec peralbuminose du liquide cephalo-rachidien sans réaction cellulaire: Remarque sur les caractères cliniques et graphiques des reflexes tendineux, Bull. et mém. Soc. méd. d. hôp. de Paris **40**: 1462 (Oct. 13) 1916.

right ear. It was for relief of the latter symptoms that he sought medical aid. The past history was irrelevant.

On examination the patient was found to be in considerable discomfort, the result of the ear pain and sore throat. The temperature was 37.7 C. (99.8 F.) and the pulse 92. The pharynx was injected and edematous. There were bulging and redness of the right ear drum. A maculopapular eruption was present over the trunk and upper extremities. There was generalized shotty lymphadenopathy. A typical chancre in the process of healing was present on the glans penis. Examination of the heart, lungs and abdomen were negative.

Laboratory examination of the blood revealed 5,080,000 red blood cells per cubic millimeter and 8,100 white blood cells, with a normal differential count. The urine and stool examinations gave negative results. The blood Wassermann and Kahn tests were 4 plus. Dark field examinations of material obtained from the penile lesion revealed Spirochaeta pallida.

On February 14 the patient was given fifteen hours of fever therapy at 41.4 C., which he tolerated very well. Dark field examinations of scrapings from the penile lesion on February 15, 16, 17 and 20 were negative for Spirochaeta pallida. Chemotherapy was started on February 25 and the patient received one injection of arsphenamine, two injections of neoarsphenamine and three injections of mercuric succinimide before his discharge from the hospital on March 2. At the time of discharge his blood Wassermann test was 4 plus in 1 : 32 dilution. The primary and secondary manifestations of syphilis had completely disappeared.

He was given 0.4 Gm. of arsphenamine on March 4. One week later, when he returned for his next treatment, he complained of pain across the lower part of the back, cramps in his legs and difficulty in walking. The onset of these symptoms apparently occurred immediately after his discharge from the hospital on March 2. A lumbar puncture done on March 14 yielded a clear, colorless spinal fluid under normal pressure. There were no cells in the spinal fluid, but the total protein content was 160 mg. per hundred cubic centimeters. The Wassermann test reported on the spinal fluid was noncholesterinized antigen ±, cholesterinized antigen 3 +, Kahn test —. The colloidal gold test showed no abnormality.

The patient was referred to the Neurological Clinic on March 15. He complained of difficulty in walking, pains in the legs and excessive perspiration of the feet. These symptoms had developed seventeen days after the fever treatment. There were no symptoms referable to the cranial nerves, upper extremities or sphincters. The patient walked, unaided, with a waddling, steppage type of gait. There was marked weakness of the flexors and extensors of both feet. He was unable to elevate the heels more than an inch from the floor when attempting to stand on his toes. The pelvic girdles and thigh muscles showed some slight weakness. There was no localized atrophy or fibrillary tremors observed in the musculature of the lower extremities. The lower tendon reflexes were hyperactive and equal. The Babinski sign could not be elicited. Deep and superficial sensations were normal. There was marked hyperhidrosis of the feet.

The patient was seen in the Neurology Clinic one month later, on April 15. He reported considerable improvement in the strength of the lower extremities but he was still unable to walk long distances without fatigue. The gait showed considerable improvement and the muscular weakness was less marked than formerly. There was the same tenderness on palpation of the popliteal spaces and also on the lateral aspects of the legs over the peroneal nerves. The tendon reflexes were still hyperactive.

A lumbar puncture done on April 22 yielded a normal spinal fluid, except for total protein content of 120 mg. per hundred cubic centimeters. The spinal fluid Wassermann and Kahn tests were negative.

On May 20 the patient reported some improvement in the motor power of the lower extremities but the gait was still abnormal. He was seen again in December 1939, and at this time the gait was normal. Reexamination in April 1940 revealed no abnormalities. The total protein content of the spinal fluid was 35 mg. per hundred cubic centimeters.

CASE 4.—J. A., a man aged 24, was admitted to the Rochester Municipal Hospital on April 14, 1939, with a diagnosis of chronic myelogenous leukemia. The disease began thirteen months before admission with hemorrhage from the gums following the extraction of several teeth. He had been treated with solution of potassium arsenite at intervals in an effort to keep the white blood cells below 1,000,000 per cubic millimeter. He complained of some numbness and tingling of the hands while taking this medication, but no muscular weakness had been noted.

On examination the patient appeared chronically ill. Vital signs were normal except for a temperature of 38.8 C. (101.8 F.). The skin showed some brownish pigmentation. There was marked enlargement of the spleen and liver. Blood studies showed a moderate normocytic hyperchromic anemia and the white blood cell count was 207,600 cells per cubic millimeter. The blood smear was typical of myeloid leukemia. The neurologic examination was negative except for loss of the achilles reflexes. The patient was given a course of high voltage roentgen therapy which resulted in decrease in the size of the spleen and reduction of the white blood cells to 75,000 per cubic millimeter. He was then discharged from the hospital on May 12 and was followed in the Blood Clinic.

On October 31 he complained of a penile lesion which had been present for about one month. Examination revealed two superficial lesions without induration of the glans penis. Dark field examination of material obtained from these lesions revealed numerous spirochetes. Blood Wassermann and Kahn tests taken at this time were negative. There were no secondary manifestations of syphilis.

The patient was readmitted to the hospital and after the routine preparation he was given fifteen hours of hyperthermia at 41.5 C. on November 6. The white blood cell count at the beginning of treatment was 119,000 and at the conclusion 120,000. No spirochetes could be found on dark field examination after five hours of fever. On November 9 the dark field examination was still negative for spirochetes. At the time of discharge, November 14, the penile lesion had healed, there were no secondary lesions and the blood Wassermann test was negative. The white blood cell count was 318,000 per cubic millimeter.

The patient returned to the clinic on November 22 complaining of sharp pains in his lower back and legs, weakness of the legs, difficulty in walking and numbness of his feet. These symptoms began eleven days following the fever treatment. The weakness of the legs was so marked that he could not climb stairs or walk on level ground without some assistance. There was no sphincter disturbance. The pains in his back and legs were increased by such acts as coughing, sneezing and straining. The abnormal neurologic signs were limited to the lower extremities. The lower tendon reflexes were absent. All muscle groups in the lower extremities were weak. He was unable to rise on his toes. His gait was waddling in type and very unsteady. The manner of arising from the recumbent position was similar to that observed in progressive muscular dystrophy. There was diminution of pain and temperature sensation over the lower third of the legs and feet, of patchy distribution. There were no pyramidal tract signs. Spinal fluid examination on November 22 was normal except for a total protein content of 79 mg. per hundred cubic centimeters. Subsequent lumbar punctures revealed total protein values as follows: December 3, 140 mg.; December 21, 130 mg.; April 26, 1940, 50 mg. At the time of his last examination, April 26, he was greatly improved although there was still some evidence of muscular weakness. The neurologic examination was negative except for absence of the achilles reflex.

CASE 5.—C. S., a woman aged 26, was admitted to Strong Memorial Hospital on Oct. 9, 1939, because of a vaginal discharge and lower abdominal pain. Four months before admission she acquired a gonococcic infection and since this time she had taken 500 Gm. or more of sulfanilamide without any improvement in her symptoms.

The patient was undernourished. Vital signs were normal. The physical examination was negative except for tenderness in both lower quadrants and erosion of the cervix and the vaginal discharge. The neurologic examination was negative.

Examination of the blood revealed 4,400,000 red blood cells, hemoglobin 12 Gm., white cells 14,100. Blood sulfanilamide was 7.5 mg. per hundred cubic centimeters. Gonococci were cultured from both the urethra and the cervix. The blood Wassermann test was negative. Urine examination was negative.

The patient was given 33 Gm. of sulfapyridine between October 13 and 21. The blood sulfapyridine content on October 18 was 5.8 mg. per hundred cubic centimeters. Cervical and urethral cultures taken two days after the sulfapyridine was discontinued were still positive for gonococci. In view of the unsatisfactory results of sulfonamide therapy, it was decided to give her fever therapy.

On October 30, after routine preparation, she was given fifteen hours of hyperthermia at 41.5 C. She withstood this procedure very well except for persistent vomiting. Cervical and urethral cultures taken on November 1, 2, 3 and 6 were negative for gonococci. She was discharged on November 6, free from symptoms.

The patient returned to the hospital on November 24 complaining of numbness and weakness of her legs and feet. These symptoms had appeared two weeks after fever treatment and were accompanied by severe pains in her lower back and legs, but they did not prevent her from working. The neurologic examination was negative, except for loss of the achilles reflexes, weakness of the legs and feet and unsteadiness of gait. There were no sensory changes. She returned two weeks later for lumbar puncture. The spinal fluid showed a positive Pandy test and no cells. The total protein was 240 mg. per hundred cubic centimeters.

At the time of her last examination, April 1, complete recovery had taken place and the total protein content of the spinal fluid was 30 mg. per hundred cubic centimeters.

CASE 6.—L. A., a man aged 46, was admitted to the Strong Memorial Hospital on Jan. 2, 1940, for treatment of tabes dorsalis with fever therapy. He gave a history of a penile lesion in 1924, which was treated with mercury inunctions and some medication by mouth over a period of three months. During the past four years he complained of sharp shooting pains in his legs, difficulty in starting the urinary stream, and incontinence of the urine at night. He had noted no disturbances of gait.

The neurologic examination was negative except for unequal pupils, which reacted poorly to light and in accommodation. The tendon reflexes were normal and there was no disturbance of deep or superficial sensibility. Physical examination was not remarkable.

Examination of the blood revealed 12.8 Gm. of hemoglobin, 3,950,000 red blood cells per cubic millimeter and 11,400 white blood cells. The differential count was normal. Urine and stool examinations were negative. The blood Wassermann test with both antigens and the Kahn test were 4 plus. Lumbar puncture yielded a clear, colorless fluid under normal pressure. There were 10 lymphocytes per cubic millimeter. The total protein content of the spinal fluid was 45 mg. per hundred cubic centimeters.

On January 5 he was given fifteen hours of fever at 41.5 + C. without complications. Following the fever treatment he was up and about the division and was discharged January 10.

He returned to the clinic February 9 complaining of weakness of his legs and difficulty in walking. The onset of his weakness was noted following his discharge from the hospital January 10. Over a period of three or four days the weakness rapidly progressed to a point where he was hardly able to walk, unable to climb stairs and unable to get out of a chair without helping himself with his arms, and it was impossible for him to stand on his toes. At no time was there severe pain in his back or legs. Paresthesias were present over the lower legs and feet.

The neurologic examination at this visit was the same as previously recorded except for absence of the right achilles reflex and diminution of the left. He walked with a waddling type of gait. He was unable to get out of a chair without helping himself with his upper extremities. It was impossible for him to climb stairs. Spinal fluid was obtained at the time of this examination, which showed 2 lymphocytes per cubic millimeter and a total protein content of 100 mg. per hundred cubic centimeters.

At the time of his last examination, May 11, there was considerable improvement in the muscular weakness of the lower extremities. The gait was practically normal. The achilles reflexes were absent. Total protein content of the spinal fluid was 45 mg. per hundred cubic centimeters.

Another case which came under observation recently might be briefly mentioned at this time:

A man aged 36 was seen in consultation because of weakness of the legs. His illness began two months previously with pains and tingling sensations in his legs. These symptoms were followed by progressive weakness of his legs which made walking difficult and climbing stairs almost impossible. There was no history of a febrile illness or ingestion of drugs prior to the onset of the neurologic symptoms.

Examination revealed marked weakness of the musculature of the lower extremities without atrophy. He was able to walk unassisted, but climbing stairs was difficult and he was unable to elevate the heels from the floor. The lower tendon reflexes were absent. There was no nerve or muscle tenderness and no sensory changes. The only abnormality of the spinal fluid was a total protein value of 200 mg. per hundred cubic centimeters. This case presented the same clinical picture as the cases already described and is regarded by us as a spontaneous case of the syndrome under discussion.

COMMENT

The six cases reported can be summarized together from the time the fever treatments were given. Each patient was given fifteen hours of fever at 41.5 C. without any unusual complication at the time of treatment or immediately thereafter. In each case there developed within a period of from ten to sixteen days (except in case 6) following fever treatment a neurologic syndrome, unaccompanied by fever, which was remarkably constant. The most constant feature was motor disturbances involving the muscles of the pelvic girdle and lower extremities resulting in a waddling type of gait which was not unlike that seen in progressive muscular dystrophy. Severe radicular pains, muscle nerve tenderness and mild dysthesias occurred in several of the cases. In no instance were there symptoms referable to the cranial nerves or sphincters. The positive neurologic signs in all cases were limited to the lower half of the body and consisted of muscular weakness resulting in a waddling gait, diminution or absence of the tendon reflexes, minimal disturbances of deep and superficial sensation, and nerve tenderness. Three of the patients complained of marked hyperhidrosis of the feet. Spinal fluid examination in six cases yielded a normal spinal fluid except for an increase in the total protein content ranging between 100 and 240 mg. per hundred cubic centimeters without any increase in the number of cells.

The analysis of these cases, aside from the similarity of the neurologic syndrome, reveals two common factors: first, a prolonged fever treatment of fifteen hours at 41.5 C. and, second, the onset of the neurologic symptoms at a definite time interval ranging between eleven and sixteen days after the treatment. Three patients in the series had taken fairly large amounts of sulfanilamide or its derivatives without evidence of toxic manifestations which could be attributed to the drug or the disease. The drug in case 1 had been discontinued for eight weeks before fever treatment was given. In case 2 it had been stopped two weeks before, and in case 5 it was discontinued a few days before fever therapy was given. Two patients had primary syphilis but only one showed a weakly positive spinal fluid Wassermann reaction for five weeks.

About the time at which we encountered the second case a somewhat similar one was reported by Ornsteen and Furst. Their patient had received about 130 Gm. of sulfanilamide over a period of about thirty-five days for the treatment of gonorrheal infection. About two weeks after the drug was discontinued he was given approximately four hours of fever therapy between 106 and 107 F. He felt much improved and gained weight until one month later, when he noticed that his hips and legs were growing increasingly weaker. He did not complain of pain in his limbs but did note patchy numbness and paresthesia. The chief neurologic signs were waddling gait, weakness of the dorsiflexors of the left foot, loss of the abdominal and left cremasteric reflex, absent achilles reflexes, hypo-active knee jerks, tenderness of muscles, and normal sensation with the exception of diminution of pin point perception below the middle third of the legs. Sulfanilamide was not detected in the blood. Examination of the spinal fluid was essentially negative. The patient left the hospital greatly improved one month after his admission because of the neurologic disorder. They concluded that this was a case of toxic neuritis with a progressive muscular dystrophy-like picture probably resulting from excessive ingestion of sulfanilamide.

The case described by Ornsteen and Furst and our cases 1, 2 and 5 were similar in many respects. The fact that fairly large amounts of sulfanilamide had been administered in these three cases made it seem logical to conclude that the drug alone, or its use prior to the fever treatment, was in some way responsible for the neurologic changes.

Prior to the advent of sulfanilamide and with routine fifteen hour treatments, a neurologic complication of the type described has not been observed in our clinic, where various amounts of fever at high temperatures have been administered in 1,100 cases. The follow-up on all of these 1,100 cases has been adequate enough to warrant the belief that no similar cases have resulted from the technic of the treatment. In recent literature many toxic effects of sulfanilamide have been described, but as a rule they appear during the administration of the drug and subside when it is discontinued. However, cases have been reported in which the toxic manifestations have been delayed. Lockwood [6] mentioned a case in which severe hemolytic jaundice developed eighteen days after the drug had been discontinued.

In view of the fact that this neurologic syndrome had never been observed to follow either form of treatment when used alone, it was thought that perhaps the combination might in some way be responsible. A few months later, however, following a routine fifteen hour fever, we observed the same syndrome in two cases of primary syphilis and one case of tabes dorsalis in which sulfanilamide had never been given. This seemed to exclude sulfanilamide as a causative agent. Likewise the technic of the fever therapy appeared unlikely as the sole cause. In this clinic several hundred cases were treated with prolonged fever, from fifteen to twenty-seven hours at 41.5 C. (106.7 F.), prior to June 1938 without any complication of this type.

Guillain believes that the syndrome which he described is of infectious origin, presumably a neurotropic virus. He also stated that in some cases it had been noted that the polyradiculoneuritic syndrome developed often after a suppurative infection. He was of the opinion that in such instances a neurotropic virus plays the principal role but acquires its virulence as a result of the primary illness. At least one virus disease, herpes simplex, seems to be activated by the febrile state (Carpenter, Boak and Warren [7]). The herpetic vesicles containing the virus develop in about 60 per cent of all cases in which fever treatment is administered. The lesion starts as an erythematous patch on the face, usually about the nose or mouth, about twenty-four to thirty-six hours after the fever. Within twelve hours a papule develops which becomes a vesicle, then a pustule and finally a dry crust, which falls off in a week or ten days, leaving no scar. Herpes simplex developed in three of the six cases under discussion.

There were several features about our cases which suggested an infectious (virus) etiology. Most important of these was the latent period between the fever therapy and the development of the neurologic symptoms. This period was fairly uniform in the six cases reported and might well represent the incubation period of a virus present in the body which became activated by fever therapy (much as seems to be the case with the herpes simplex virus). We were also impressed by the fact that all the cases were encountered over a period of slightly less than two years, an observation which might indicate that a virus capable of producing the neurologic disorder was prevalent during this time. Additional evidence in favor of this idea is the increase in number of spontaneous cases which we have observed during the same period. These cases differed from those under discussion in that the paralysis was more extensive, the course more protracted and the protein content of the spinal fluid considerably higher. We might regard the cases discussed as mild or abortive forms of the syndrome. In the cases reported, animal inoculations with spinal fluid gave negative results. In 1936 Gilpin, Moersch and Kernohan [8] reported a large series of cases of polyneuritis with albuminocytologic dissociation and called attention to the increasing incidence of the disorder. It was their impression that the condition was due to a virus that had a predilection for the peripheral neuron.

The prognosis in these cases has been favorable for recovery. Pain and tenderness of the nerves and muscles subsided within a week or two. However, the return of muscular power takes much longer and it is usually from four to six months before the gait returns to normal. The abnormality of the spinal fluid is likewise slow in clearing.

Treatment of these cases consisted of the usual therapy for cases of polyneuritis due to other causes (relief of pain, rest of muscles and so on).

SUMMARY AND CONCLUSIONS

1. Six cases of polyradiculoneuritis with hyperalbuminosis of the spinal fluid followed the use of sulfanilamide and general hyperthermia.

2. Analysis of these cases would seem to eliminate sulfanilamide and hyperthermia per se as the cause of the syndrome.

3. It would seem that the disorder is the result of the activation of some infectious agent, perhaps a virus, by the fever.

6. Lockwood, John S.; Coburn, Alvid F., and Stokinger, H. E.: Mechanism of the Action of Sulfanilamide, J. A. M. A. **111:** 2259 (Dec. 17) 1938.

7. Warren, Stafford L.; Carpenter, Charles M., and Boak, Ruth A.: Symptomatic Herpes, a Sequela of Artificially Induced Fever, J. Exper. Med. **71:** 155-168 (Feb.) 1940.

8. Gilpin, Sherman F.; Moersch, Frederick P., and Kernohan, James W.: Polyneuritis, Arch. Neurol. & Psychiat. **35:** 937 (May) 1936.

ABSTRACT OF DISCUSSION

ON PAPERS OF DR. DE JONG AND DRS. GARVEY, JONES AND WARREN

DR. LOUIS CASAMAJOR, New York: Much confusion has existed concerning the term "Landry's paralysis." It was early believed to be a form of subacute poliomyelitis but later work showed that progressive ascending paralysis was not occasioned by a progressive ascending inflammatory reaction in the anterior central gray matter. The clinical course of these cases with complete recovery of a large majority taught that the lesion was not one of destruction of the anterior horn cells. Obviously some reversible process must exist as the basis of acute ascending paralysis. The pathologic observations which Dr. De Jong reports in his cases were practically identical with those of the two cases I reported in 1919. The differences were of degree and not of kind. I was convinced that the primary lesion was an inflammatory one in the arachnoid affecting primarily the nerve roots where they run in the arachnoid. The peripheral nerve changes and those in the anterior horn and spinal ganglion cells are secondary to interruption of nerve fiber function by the arachnoid inflammation. The situation was somewhat similar to tabes as described by Nageotte and it is interesting that in tabes with a productive arachnoiditis the changes are almost entirely in the sensory roots. In the acute ascending paralysis there is likewise an arachnoiditis but not a productive one, and for some unknown reason the changes are more in the anterior roots. When my cases were reported I was unaware of the article of Guillain-Barré and Strohl, which had been published three years earlier. Spinal punctures could not be done in my cases as they were observed under conditions of active warfare, and had the spinal fluid been obtained there were no facilities for determination of total protein. In the cases seen more recently the albuminocytologic dissociation described by these authors was present in all. Dr. De Jong included in his paper two cases in which, for good reasons, lumbar puncture was not done. In the second case of his series there was a definite albuminocytologic dissociation. The existence of the high protein and low cell count in the spinal fluid is to my mind a valuable finding. I feel it is the spinal fluid expression of the inflammatory changes in the arachnoid which I believe to be the basic cause of the condition. The existence of such a reaction differentiates the condition from poliomyelitis on the one hand and peripheral neuritis on the other. Were this a real anterior horn cell degeneration due to poliomyelitis, one would certainly expect to find the meningeal reaction which gives the increase of cells with not such a great increase of protein. That fact alone proves that the pathologic change responsible for this condition exists inside the dural sac. The term "Landry's paralysis" could be dropped without much loss to our nomenclature.

DR. PETER BASSOE, Chicago: I wish Dr. De Jong had taken more time to describe that type of lesion. It perhaps represents a clinical entity which we will understand better when we know more about viruses. When it comes to his discussion of terminology, I cannot follow him. The term "Landry's paralysis" is obsolete and confusing, whether Landry's case was one of beriberi, as claimed by Dr. Madelaine Brown, or a cord infection similar to the one described by Dr. De Jong. The term "acute ascending paralysis" (ascending must mean ascending, whether one thing or another; we can't change the English language) is useful as designating a syndrome which is fairly common on account of the segmented structure of the cord. Any disease starting in the lower part of the cord with sufficient momentum to travel upward may produce an ascending paralysis, and I don't see any reason why we should not call it all ascending paralysis, which of course makes it a syndrome only. And I don't see why we shouldn't say that, when ascending paralysis is caused by poliomyelitis, that is also ascending paralysis. Less common are the kinds of myelitis described by Dr. De Jong today. Perhaps they are commoner than we think. Then there are the kinds of spinal root and ganglion inflammation that have been described by Pette and Környey and more recently by Peters and Scheid. Rabies, rabies vaccine paralysis and tick paralysis may be acute ascending; and we may have ascending leptomeningeal, dural and epidural inflammations and so on. The day I left home I saw for the first time Wilson's magnificent two volume textbook. I looked up what he said about Landry's paralysis, and as most of you may not yet have seen the book I will quote some of his statements: "As a technical term Landry's paralysis lacks precision, etiological or pathological, and its clinical worth is a little dubious. The name lingers on, none the less, bearing witness to the fact that clinical types of acute ascending paralysis are not uncommon and that knowledge of their causation is still at times rudimentary." Wilson considers it a mistake to confine the syndrome to the motor system. He included poliomyelitis, also ascending myelitis, in the spinal disorders. He says "As has often happened in medicine, the first conception has been widened and a host of cases included of which perhaps only a few strictly conform to it. On the pathologic side, too, variations have been numerous enough to render a unitary acute ascending paralysis impossible." Then finally he adds something pertinent to what Dr. De Jong has said today, namely "For some obscure reason several writers today seek to restrict Landry's paralysis to the acute ascending toxicosis of ventral horn cells" (without inflammation).

DR. A. M. ORNSTEEN, Philadelphia: In the group of cases reported by Dr. Garvey and his co-workers there can be no question about its similarity to the Guillain-Barré syndrome because of the acute onset with a uniformity of clinical picture as he described involving the lower extremities and the cytoalbumin dissociation which has been consistently held as a differential finding in this form of multiple or polyneuritis. In an experience of 1,150 cases of fever therapy, given I presume under similarly controlled conditions over a period of ten years, Dr. Garvey and his co-workers have not seen such a complication, but in the past two years they have seen six cases under identical conditions of the fever treatment with a period of incubation of from ten to sixteen days, followed by weakness of both lower limbs, pain in the back, severe in some cases, various reflex and sensory changes and with the spinal fluid feature already mentioned. They did not conclude that fever therapy was the cause of it; neither could they conclude that sulfanilamide would produce the neuritis, for obvious reasons, and their conclusion that the virus was activated by fever I believe is acceptable unless some one can give a reason why such a situation does not occur occasionally in the situation in which patients harbor a virus and their resistance to that virus is altered by certain physical factors. It has been well known that neuritis is often attributed by the patient and the physician to a certain physical factor, exposure frequently the offending factor; and there are people who still believe that such a common peripheral neuritis as Bell's palsy is caused by exposure, whereas others believe that the particular individual who develops a Bell's palsy must have some factor in the background which makes that nerve vulnerable to exposure; hence Dr. Garvey's interpretation that activation of a virus in the host may be produced under certain conditions, at present not understood, by fever. Since it did not happen in the first eight years of the decade of his survey and it has in the last two years, it would be interesting to determine whether or not in his community there were an equal number of cases, not just the one other case which he saw in which no sulfanilamide or fever therapy was given, that showed a development of the Guillain-Barré syndrome. That would be more convincing; the increased incidence of the disease would explain the increased number of carriers of the virus and, under certain conditions, such as hyperpyrexia in Dr. Garvey's cases, exposure to cold, or a background of vitamin deficiency, infectious polyneuritis may be precipitated.

DR. FREDERICK P. MOERSCH, Rochester, Minn.: We have more or less dropped the term "Landry's paralysis" because we do not know the etiology of the condition. Once we discover the exact etiology of "Landry's paralysis" a reclassification of these conditions will be easier. As far as I know, we have seen no case of peripheral neuritis or polyradiculoneuritis resulting from sulfanilamide therapy. We have observed cases of peripheral neuritis resulting from preparations related to sulfanilamide. The fact that neurologic complications so rarely follow the use of sulfanilamide I believe is good evidence that in Dr. Garvey's cases the sulfanilamide

probably had no relation to the onset of the symptoms. Regarding fever therapy, we have observed one instance of polyradiculoneuritis following from therapy. It was interesting that this patient, because of an acne, had received a preparation containing tin just prior to the fever therapy and sulfanilamide. We were unable to determine in our own minds whether the neuritis or polyneuritis was due to tin, to fever or to some unknown factor. Some time later when we went through what seemed to be a wave of polyradiculoneuritis we instituted fever therapy in these cases with poor results, and we concluded that fever therapy in cases of polyneuritis was rather harmful. Dr. Krusen of our staff has called to my attention a report by Dr. Gwynn of Washington, who reported four cases of peripheral neuritis following fever therapy. At the same time, in the same city but in another hospital, and using a little different type of fever therapy, there were observed fourteen cases of peripheral neuritis following fever therapy. I have seen the records of some of those patients and I am inclined to believe that they represent a polyradiculoneuritis as described by Dr. Garvey and his co-workers. The large number of cases of peripheral neuritis occurring in one locality suggests the possibility of some infectious basis. As noted by Dr. Garvey, the usual sequence of events in a case of polyradiculoneuritis is an infection, a latent period, and then the development of a polyradiculoneuritis, suggesting the presence of a common denominator as a virus. There are many cases in which no infection or infectious history is obtainable, and I have been wondering whether polyradiculoneuritis may not after all be another syndrome rather than a disease entity resulting from a specific virus.

DR. A. E. BENNETT, Omaha: I should like to inject into this discussion of cases involving the so-called Landry syndrome the possibility that some of them resemble curare poisoning. Of the cases I have seen, an almost pure flaccid motor paralysis develops in most and death occurs from asphyxia. However, when recovery occurs it is rapid. In one recent case recovery occurred within a few days after the paralysis became complete, including the respiratory muscles. Prostigmine and thiamine were used in treatment. It seems that there is some evidence to show that perhaps faulty neuromuscular function with a lack of acetylcholine may be a factor in this syndrome. With respect to Dr. Garvey's cases, almost any clinic that has given large numbers of fever therapy treatments has seen this complication. Dr. Garvey's patients were given long fever therapy heatings of ten hours or more. I doubt the idea of virus infection being responsible for this disorder. Anoxia and thiamine deficiency are more likely causative factors. Weaver, formerly of Ohio State and now of Detroit, has definitely produced peripheral neuritis in animals with fever therapy and anoxia. Since we discovered this condition we have given all our patients prophylactically large doses of thiamine and throughout the long heatings they get oxygen. As Dr. Moersch told you, in the large number of treatments given at the Mayo Clinic they have seen only one case, and it has been routine for Dr. Krusen to use continuous oxygen inhalation with fever therapy. It may be that sulfanilamide is also a factor in the production of anoxia and finally polyneuritis.

DR. NORMAN JOLLIFFE, New York: I should like to bring out a point that may account for the development of polyneuropathy following fever therapy. It was shown several years ago by Cowgill that the vitamin B_1 requirement increased with an increase in total metabolism. The administration of fever therapy over a period of ten hours every day or every other day must increase the total metabolism markedly, and with it a parallel rise in the thiamine hydrochloride requirement. It would not be inconceivable that the vitamin B_1 requirement of these individuals was doubled, and unless dietary precautions were taken to increase the B vitamins it is likely that with the increased requirement due to fever therapy their diet was inadequate in vitamin B_1. The ten to fourteen day period mentioned by Dr. Garvey could as well be the time required to develop a polyneuropathy due to a vitamin B_1 deficiency as to an incubation period of an infection. I should like to ask a question concerning the cell counts in Dr. Garvey's patients. I believe that in about one half of his patients absolutely no cells were found in the spinal fluid. Did he not mean to indicate that there was no increase in cells?

DR. PAUL C. BUCY, Chicago: Dr. Jolliffe, I should like to ask whether or not you would expect this alteration in protein content in the spinal fluid with thiamine hydrochloride deficiency?

DR. JOLLIFFE: Certainly not, as a rule. We have, however, seen increased protein in the spinal fluid in patients having thiamine hydrochloride deficiency, though it occurs rarely. Whether the increased protein was due to B_1 deficiency or not, I have no proof. Since thiamine hydrochloride deficiency is not limited to the peripheral nerves but includes changes in the roots and spinal columns as well, it is theoretically possible that an increased protein content might result from thiamine hydrochloride deficiency.

DR. MOERSCH: In a postdiphtheritic polyneuritis in which there is an increase in the total protein, would that fit in with this? I was wondering what your experience might be.

DR. JOLLIFFE: I have never seen an acute postdiphtheritic neuritis, but it would fit in with this explanation.

DR. IRVING J. SANDS, Brooklyn: Those of us who have had the opportunity of following the various types of encephalitis during the past years have been impressed with the increase in the number of patients of the type described by the readers of the last two papers. Dr. De Jong's cases brought to my attention a group of patients we have had the privilege of following in Dr. Riley's division at the Neurological Institute. They have been described as diseases due to virus infection, manifested clinically by an ascending type of paralysis. Those cases which came to necropsy showed a difference in the pathologic condition though clinically they showed an almost identical course. I recall two patients who had a definite ascending paralysis with death resulting in about six to ten days after the onset of the illness. In one patient multiple areas of demyelinization was found, and in the other nothing except slight cloudy swelling and chromatolysis were detected. During the past four years I have had the opportunity of following a group of cases at the Kingston Avenue Hospital for Contagious Diseases. They presented a symptomatology as shown by Dr. Garvey's patients. However, they had a much larger total protein in the spinal fluid, usually between 200 and 350 mm. In the majority of these cases there was a history of a mild upper respiratory infection preceding the onset of the neurologic signs. In the past two years we have been giving them large doses of thiamine hydrochloride. It has been my impression that thiamine hydrochloride therapy has made no difference in the speed or the extent of the recovery. What is the etiology of these cases? I believe that it is due to a virus infection, though I have no definite proof. It is the opinion of many who have studied the manifestations of encephalitis and encephalomyelitis that the virus agents comprise a large group like the pneumococci, that eventually these different groups will be differentiated and recognized, and that each type of virus will be proved to have a special predilection for invasion of a particular part of the nervous system producing the different clinical types of neurologic disorders with which we are now familiar clinically.

DR. DONALD SHASKAN, New York: In a period of less than two years we have followed eight cases of the Guillain-Barré syndrome in Dr. Foster Kennedy's service at Bellevue. I should like to ask Dr. Garvey two questions: Guillain has stipulated that from 1,000 to 2,000 mg. of total protein was necessary for the diagnosis of this syndrome, and I wondered what Dr. Garvey thinks of this quantitative differentiation as a factor in diagnosis. The second question is Why should no virus have been recovered in any of these cases, either Dr. Garvey's cases or any cases in the literature?

DR. A. M. RABINER, Brooklyn: I had not intended discussing these cases until some of the discussers attempted to blame fever therapy for the development of these clinical syndromes. On a number of occasions spinal fluid examinations of patients who did not have any evidences of polyneuritis, polyradiculoneuritis or meningo-encephalomyelitis, who in the course of an upper respiratory infection seemed somewhat drowsy, had spinal fluid study performed which revealed an

increased total protein. We also know that virus infections causing the so-called common cold produce a varying type of clinical picture. Sometimes there is only a tracheitis, at other times more widespread involvement of the respiratory apparatus. In other words, we know that virus infections that do not involve the central or peripheral nervous system may produce a protean type of implication of the system in general. Some years ago when Dr. Strauss and I reported a group of these cases we called them, for want of a better name, myeloradiculitis. In reviewing the literature we found reports of similar clinical syndromes from all over the world with many names attached to them, indicating varying diffuse anatomic involvement, at times limited to the brain, at other times affecting also the meninges, sometimes limited only to the cord and often implicating all the structures from the peripheral nerves up the roots, to the brain. The names given to these syndromes were usually purely anatomic designations of the structures involved. One of our patients subsequently developed a parkinsonian syndrome and this suggests an etiology similar to that causing epidemic encephalitis. Here then Dr. Garvey reports a group of six cases occurring within a short period of time under the same type of fever therapy regimen that has been given to their patients in previous years. Now for the first time six cases appear with this clinical picture. To blame the fever therapy for this I think is a far fetched speculation. These are undoubtedly cases in which there was a virus infection of the nervous system during the period fever therapy was being administered.

DR. RALPH HAYWARD, Toronto: I want to mention about 150 cases of ascending paralysis that I saw in West China. These cases all seemed to occur in a region of about 20 miles radius. Cities 100 miles away had none at all. The onset was sudden, with a little nausea and vomiting, the symptoms appeared in about five or six hours, and recovery would occur in three or four days. About 5 per cent of the patients died within forty-eight hours. The peculiar thing was that the inhabitants of the city did not seem to be bothered, but after the war with Japan a national university came to our city and the students came down with it in large numbers; I don't know whether it was from eating the same things or from respiratory infection. Just as I came away this April there were several camps for wounded soldiers where the men were coming down in large numbers with this same disease.

DR. RUSSELL N. DE JONG, Ann Arbor, Mich.: It was desirable that my paper on acute ascending paralysis and Dr. Garvey's paper on the Guillain-Barré syndrome be discussed together, because clinically these two conditions are similar and they may represent different stages or degrees of the same disorder. I have been studying a group of cases, seen in the University Hospital in Ann Arbor, which conform closely to those described by Guillain and Barré, but I disagree with the French authors in certain respects. In their terminology of the syndrome they use the word "curable" polyradiculoneuritis. If the syndrome is to be diagnosed by the presence of albuminocytologic dissociation, I am sure that not all cases are curable. I have observed some cases that conformed to the descriptions of Guillain and Barré but had a chronic course and others that terminated fatally. The condition is certainly more than a peripheral neuritis, as in some cases a facial paralysis has been noted, others have shown evidence of a brain stem or bulbar paralysis, and papilledema has been noted in certain instances. Paralysis of the bowels or bladder is not unusual. The cases that terminate fatally are similar to those that I have described today as cases of acute ascending paralysis, and it is my impression that these all are members of the same group of disorders. If that is the case, we shall have to enlarge or broaden our concept of the term "polyradiculoneuritis" as described by Guillain and Barré, noting that the prognosis is not favorable in all cases—not all are curable, and some terminate fatally.

DR. PAUL H. GARVEY, Rochester, N. Y.: In reply to Dr. Ornsteen, at the present time we have two patients in the hospital that have total protein contents one of 800 and one of 600, and since this paper was written we have had three more cases following fever therapy. Perhaps this protein is due to edema and vascular congestion at the time of the fever treatment. However, we have done routine punctures on the last three patients that developed the same syndrome and the total protein content of fluid was within normal limits three days after the treatment, so presumably that abnormality develops later and cannot be directly related to the fever. It was suggested by Dr. Bennett that it was due to anoxia and perhaps to the fever treatment. Prior to two years ago we treated patients for twenty-seven hours and many patients have been treated more than fifteen hours without anything of this sort developing, so that I should think if it were on that basis these cases would have occurred before two years ago. With regard to this being a vitamin deficiency or the development of an acute deficiency, it has been our experience that large doses of thiamine hydrochloride have not been effective in the treatment of these cases. In the neuritis associated with chronic alcoholism, which is a good example of a deficiency neuropathy, the total protein content of the spinal fluid is not appreciably elevated. The cell counts were taken from the records recorded by the house officers. Of course from ten to fifteen years ago a cell count of ten was said to be normal; now we know that anything above five is considered abnormal, so that so far as the chart was concerned I would just as soon have one, two, three or four cells on that chart as none. Guillain in his recent article insists that 1 or 2 Gm. of protein must be present in the spinal fluid in order to make the diagnosis. I think it seldom attains that level. He mentioned in his article that when the spinal fluid protein is lower than 1 or 2 Gm. they must be considered as abortive cases. It is interesting that about two weeks ago in THE JOURNAL Stone and Aldrich reported two cases of this syndrome in which albuminocytologic dissociation was a late development.

THE EFFECT OF DISTENTION OF ABDOMINAL VISCERA

ON THE CORONARY BLOOD FLOW AND ON ANGINA PECTORIS

N. C. GILBERT, M.D.
G. K. FENN, M.D.
AND
G. V. LEROY, M.D.
CHICAGO

The incidence of anginal pain following the ingestion of food has been commented on by most of the writers on angina pectoris, beginning with Heberden,[1] who stated that "those who are afflicted with it are seized while they are walking, and more particularly if they walk soon after eating." Osler,[2] in his monograph on angina pectoris, states "Of the exciting causes there are three important elements: muscular exertion, mental emotion and digestive disturbances. . . . As an attack ends, the patient may belch quantities of gas or pass flatus from the bowel, both with apparent great relief." So marked is the association of pain with upper digestive tract symptoms that Verdon[3] and later the Jacksons[4] considered that the pain was of neuromuscular origin, consequent on gas under pressure in a hollow viscus.

The increased incidence of anginal pain after meals is explained in part by the increased work required

Read before the Section on Practice of Medicine at the Ninety-First Annual Session of the American Medical Association, New York, June 13, 1940.

1. Heberden, William: Some Account of a Disorder of the Breast, M. Tr. College of Physicians **2**: 59-67, 1786.
2. Osler, William: Lecture on Angina Pectoris and Allied States, New York, D. Appleton & Co., 1897.
3. Verdon, Walter: Angina Pectoris, London, Baillière, Tindall & Cox, 1920.
4. Jackson, D. E., and Jackson, Helen L.: Experimental and Clinical Observations Regarding Angina Pectoris and Related Symptoms, J. Lab. & Clin. Med. **21**: 993-1006 (July) 1936.

of the heart during digestion. This of itself demands an increased coronary flow, and the vessels may not be able to supply this demand even without the added factor of exertion. But this does not explain the effect of gaseous distention of the stomach in causing anginal attacks or the relief offered by belching. And it does not explain the influence of abdominal distention.

There is both clinical and experimental evidence to indicate a reflex vasoconstriction of the coronary arteries consequent on some stimulus arising in the viscera or elsewhere. Huchard [5] predicated a reflex angina, and Daniélopolu [6] considered that a coronary vasoconstriction could result from a stimulus originating in the thoracic cavity. Anrep [7] showed a reflex decrease in coronary flow with an increase in the intracephalic pressure, and Stella [8] showed that this was produced by means of the carotid sinus. Manning, McEachern and Hall [9] showed that there was a reflex vasoconstriction following sudden occlusion of other coronary branches. De Takats, Beck and Fenn [10] presented evidence indicating a reflex vasoconstriction of coronary arteries following pulmonary embolism. Von Bergmann [11] showed a reflex vasoconstriction of the coronary arteries following gastric distention, and Rein [12] showed that there was some constant vagal tone present in the coronary arteries and that constriction resulted from vagus stimulation.

There would seem to be abundant experimental evidence to indicate that stimulation of the vagus does result in vasoconstriction of the coronary vessels. This is amply reviewed by Anrep [13] and by C. W. Greene.[14] As Greene states, however, the reaction of the coronary vessels to stimulation cannot be predicted because of the close morphologic and physiologic association of the vasoconstrictor and vasodilator pathways. In order to prove the hypothesis of vagal origin of the vasoconstrictor fibers, he performed a series of crucial experiments in which he completely severed the vagal neurons from the coronary vagosympathetic pathways. This he accomplished by sectioning the vagus at its exit from the jugular foramen and carried on a series of physiologic experiments after degeneration of the vagus fibers. Dogs with such section of the vagus showed a loss of coronary constriction on cervical vagal-sympathetic stimulation.

In some earlier work with Prof. C. W. Greene in 1925, one of us had observed a decrease in coronary flow on distention of the stomach or the free abdominal cavity, measuring the flow with a Morovitz cannula. The results were not constant and were not published because of the fear that a factitious element might be present. The work was later repeated by Gilbert and Fenn with similarly inconclusive results. In both cases, lack of constant results can be ascribed to the type of anesthesia used, to the fact that anesthesia was carried to the point at which reflexes would tend to be abolished, and to too strong a stimulus. The Morovitz cannula method is also not as well adapted to this work as is the Rein thermostromuhr. A change in the relative position of the heart may mechanically cause a decrease in flow.

Hinrichsen and Ivy [15] also were unable to find a vasoconstrictor effect on the coronary artery with visceral stimulation but found it possible to show a vasodilator effect.

A short time ago we [16] reported on some experimental work in dogs which indicated that moderate distention of the stomach could cause a reflex constriction of the coronary arteries. Under light anesthesia a thermostromuhr was applied to the circumflex branch of the left coronary artery. The chest was closed and continuous photographic records were made of the coronary flow, together with blood pressure and pulse readings.

TABLE 1.—*Experiments on Visceral Distention*

Part Distended	Number	Coronary Artery Flow: Decreased	Increased	No Change
Lightly Anesthetized Dogs				
(Before atropine: 2 mg./Kg.)				
Stomach	12	8	1	3
Gallbladder	7	2	2	3
Peritoneum	6	3	3	0
(After atropine: 2 mg./Kg.)				
Stomach	11	1	5	5
Gallbladder	6	1	2	3
Peritoneum	4	0	3	0
Unanesthetized Dogs				
(Before atropine)				
Stomach	3	3	0	0
(After atropine)				
Stomach	2	0	1	1

Moderate distention of the stomach caused a decrease in the coronary flow without fall in blood pressure. The decrease was greater when the distention affected primarily the cardiac end of the stomach, as was observed by von Bergmann [11] in similar experiments. Section of the vagus or administration of atropine abolished the reflex. Distention of the free abdominal cavity with air also resulted in a decreased coronary flow, which again did not appear after vagus section or atropine. Since these experiments were reported, a similar series of experiments have been made on unanesthetized dogs which had previously had a thermostromuhr attached to the circumflex branch of the coronary artery under aseptic conditions, with perfect recovery. The results were essentially the same.

The results of the distention of the stomach and abdominal cavity in the anesthetized dogs and the results of the distention of the stomach in the unanesthetized dogs before and after the injection of atropine are shown in table 1. The results of the gallbladder experiments are not conclusive as far as they have been carried out. The work will be amplified and reported on later.

5. Huchard, Henri: Traité clinique des maladies du coeur et des vaisseaux: Leçons de clinique et de thérapeutique des cardiopathies artérielles, ed. 2, Paris, Gaston Doin & Cie, 1893.

6. Daniélopolu, D.: L'angine de poitrine et l'angine abdominale, Paris, Masson & Cie, 1923.

7. Anrep, G. V.: Lane Medical Lectures: Studies in Cardiovascular Regulation, Stanford University, Calif., Stanford University Press, 1936.

8. Stella, G.: Some Observations on the Effect of Pressure in the Carotid Sinus upon the Arterial Pressure and upon the Coronary Circulation, J. Physiol. **73**: 45 (Sept.) 1931.

9. Manning, G. W.; McEachern, C. G., and Hall, G. E.: Reflex Coronary Artery Spasm Following Sudden Occlusion of Other Coronary Vessels, Arch. Int. Med. **64**: 661-674 (Oct.) 1939.

10. de Takats, Geza; Beck, W. C., and Fenn, G. K.: Pulmonary Embolism, Surgery **6**: 339 (Sept.) 1939.

11. Von Bergmann, G.: Das "Epiphrenale Syndrom," Seine Beziehung zur Angina Pectoris und zum Kardiospasmus, Deutsche med. Wchnschr. **58**: 605-609 (April 15) 1932.

12. Rein, Hermann: Die Physiologie der Herz-Kranz-Gefässe, Ztschr. f. Biol. **92**: 115-127, 1931.

13. Anrep, G. V.: The Regulation of the Coronary Circulation, Physiol. Rev. **6**: 596-629 (Oct.) 1926.

14. Greene, C. W.: The Nervous Control of the Coronary Circulation, South. M. J. **29**: 478-485 (May) 1936.

15. Hinrichsen, Josephine, and Ivy, A. C.: Effect of Stimulation of Visceral Nerves on Coronary Flow in Dogs, Arch. Int. Med. **51**: 932-937 (June) 1933.

16. Gilbert, N. C.; LeRoy, G. V., and Fenn, G. K.: The Effect of Distention of Abdominal Viscera on the Blood Flow in the Left Circumflex Coronary Artery of the Dog, Am. Heart J., to be published.

In order to extend these observations on gastric distention to patients with angina of effort we had recourse to the method devised by Levy.[17] This method consisted in allowing a patient to breathe an oxygen-poor mixture until pain occurred. It was safe, because at the first sign of pain 100 per cent oxygen was administered with immediate and complete relief. It was of interest that the patients stated that after a spontaneous attack of angina they felt some depressing effect for hours. However, after these induced attacks, followed at once by oxygen administration, they stated that they felt better than before the attack.

TABLE 2.—*Abstracts of Histories of Patients*

	1. J. B.	2. G. L.	3. A. K.
Name			
Age	70 years	51 years	57 years
Diagnosis	Arteriosclerosis; heart disease	Syphilitic aortitis; arteriosclerosis; heart disease	Syphilitic aortitis; arteriosclerosis; heart disease
Blood pressure	208/110	150/68	160/74
Heart size	51%	42%	55%
Left ventricle	9.8 cm.	10.0 cm.	12.0 cm.
Electrocardiogram: PR	0.28	0.18	0.22
QS	0.08	0.06	0.06
QT	0.40	0.36	0.34
T_1	Inverted	Low	Low
T_2	Low	Normal	Low
T_4	Inverted	Normal	Normal
ST	Slightly depressed	Normal	Normal
Duration of angina	3 years	4 years	3 years
Severity	++++	++	+++

The method as used by us consisted in allowing the patient to breathe 10 per cent oxygen and 90 per cent nitrogen while lying quietly in bed and after a thirty minute rest period. The patient was instructed to indicate the moment he felt his typical anginal pain. The procedure was repeated on successive days until the patient became accustomed to the method and the control pain time became stabilized. After the control pain time had been determined, the procedure was repeated ten minutes after the ingestion of a moderately large meal and the pain time again recorded. Subsequently the second procedure was repeated after atropine in doses of one-fiftieth grain (0.0013 Gm.) had been injected intramuscularly just preceding the meal. The period required to produce pain in this instance was recorded. Several determinations of each of these pain times were made.

TABLE 3.—*Experiments on Conscious Dogs*

Thermostromuhr on Circumflex Branch, Left Coronary Artery
Change in Coronary Flow

Dog	Effect of Feeding	Time After Feeding
T-1	— 5%	5 min.
	—10%	20 min.
	+ 5%	15 min.
	+ 3%	15 min.
	+10%	15 min.
	0%	10 min.
T-3	+ 5%	10 min.
	— 5%	20 min.
	+ 5%	15 min.
T-5	0%	10 min.
	+ 8%	15 min.

Note: Each percentage change listed represents a separate feeding, on separate days.

The patients, three in number, were hospitalized for the several days required for the investigation, were known subjects of anginal pain and were removed from all medication for several days preceding the tests. They were selected from a large group of patients because of the constant character of their angina. All three complained initially that exertion after meals produced pain much sooner than was usual at other times. These three also reported that ingestion of certain foods, such as cabbage, sauerkraut, onions and other indigestible foods, was generally followed by an attack of angina. In all of them the angina, of course, varied in degree, but the more severe attack was of the classic Heberden variety. Each of the patients, prior to entering the hospital for this investigation, had obtained marked relief from his anginal symptoms by the faithful use of theophylline with ethylene diamine in doses of from 0.6 to 1 Gm. daily. On withdrawal of the drug, each of these patients had a prompt recurrence of frequent anginal pain. The pertinent data relative to the patients are shown in table 2.

TABLE 4.—*Tolerance of Anoxemia Produced by 10 per cent Oxygen, 90 per cent Nitrogen*

Summary of Data	Subjects		
Items	1. J. B.	2. G. L.	3. A. K.
All tests before eating; average	13:10	5:42	11:55
All tests after eating; average	10:45	3:25	7:45
Change after eating	—19%	—40%	—35%
Tests before eating, after atropine; average	12:40	7:36	.....
Change before eating, after atropine, average	—3.7%	+33.0%	.....
Test after eating, after atropine, average	12:30	6:28	14:42
Change after eating, after atropine: (Test after eating, after atropine / All tests after eating) in %	+17%	+87%	+93%
Change after eating, after atropine: (Test after eating, after atropine / All tests before eating) in %	—5%	+12%	+24%

The effect of the ingestion of food on the pain time is shown in chart 1.

The control pain time is plotted at 100 per cent, no attention being paid to the actual number of minutes required to produce pain. In a similar manner the pain time following ingestion of food and later following ingestion of food plus atropine is plotted in percentages of the control time. The actual time required to produce pain by the respiration of 10 per cent oxygen and the changes produced by food and atropine were quite different in each patient, and these figures are shown elsewhere (table 4).

Patient 1 (J. B.) found that the pain time following the ingestion of food was 19 per cent less than the control time. That is to say, his tolerance for 10 per cent oxygen was reduced by about one fifth. In a similar way patient 2 (G. L.) showed a reduction of 40 per cent and patient 3 (A. K.) a reduction of 35 per cent. We believe that these results demonstrate that the ingestion of a meal considerably increases the susceptibility to anginal pain in these anginous patients.

The effect of atropine on the pain time following the ingestion of food is shown in chart 2. Atropine

17. Levy, R. L.; Bruenn, H. G., and Williams, N. E.: The Modifying Action of Certain Drugs (Aminophyllin, Nitrites, Digitalis) on the Effects of Induced Anoxemia in Patients with Coronary Insufficiency, Am. Heart J. **19**: 639-654 (June) 1940.

lengthened the after meal pain time of patient 1 by 17 per cent. In comparing the pain time after food and atropine with the control time it will be seen that they are nearly the same. Actually the pain time after food and atropine was 5 per cent less than the control time. Atropine increased the after meal pain time of patient 2 by 87 per cent, which was enough to make it 12 per cent greater than the control pain time. Atropine increased the after meal pain time of patient 3 by 93 per cent and brought it up to 24 per cent above the control time.

Chart 3, in which the pain time after food plus atropine is plotted against the pain time after food alone, shows these results in a somewhat more striking fashion. The results would seem to indicate that atropine successfully interferes with the mechanism that increases the susceptibility to anginal pain after meals. It is our belief that this interference is due to inhibition of vasoconstrictor impulses that are mediated through the vagus nerve.

It has been stated [18] that a considerable increase in the coronary flow follows the ingestion of food. In our own laboratory we were unable to observe any appreciable increase in coronary flow within the time limits of these experiments.

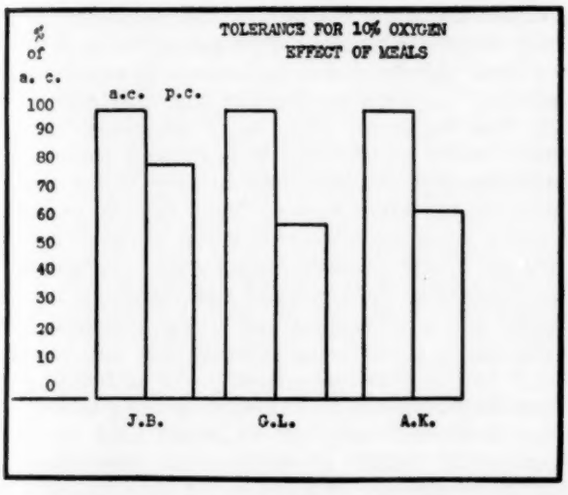


Chart 1.—The time each subject tolerated the 10 per cent oxygen inhalation before meals is represented as 100 per cent in the left hand column of each group, labeled a. c. The time the gas mixture was tolerated after meals is represented in the right hand column, marked p. c.

The effect of the ingestion of food in varying times up to twenty minutes following the meal is shown in table 3. The occurrence of anginal pain following meals has been explained by many writers as due to the inability of the anatomically damaged vessels to meet this demand and that the anatomic damage was the only factor involved. While this is true in many cases, we believe that in many other cases increased vagal tone, or a vasovagal reflex, as described by Weiss and others, plays an important part in the production of pain. Atropine has long been mentioned as an instrument to increase the coronary flow, but no one has been impressed with the significance of this observation. Essex and his co-workers [18] comment on this in a recent article in which they show an increase of 86 per cent in the intact conscious dog after atropine.

The effect of atropine alone on the low oxygen tolerance in two of the patients who were investigated is shown in chart 4. With patient 1 atropine alone made

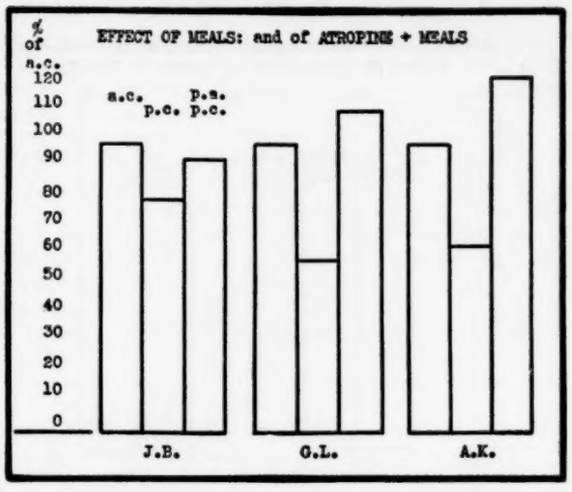


Chart 2.—The tolerance for 10 per cent oxygen before meals is represented in the left hand column of each group as 100 per cent and is labeled a. c. The tolerance for the gas mixture after meals is depicted in the middle column, labeled p. c. The right hand column represents the tolerance after atropine, after meals, and is marked p. a. p. c.

almost no difference. There was actually a reduction of 3.7 per cent in the pain time after atropine. Reference to table 2 will show that patient 1 was a 70 year old man with hypertension and cardiac enlargement. From the physical examination alone, one would suspect the presence of considerable anatomic change in the heart. This, together with the atropine response shown in chart 4, would indicate that the vagal tone was not as important a factor in the production of pain as with patient 2, whose pain time after atropine was increased

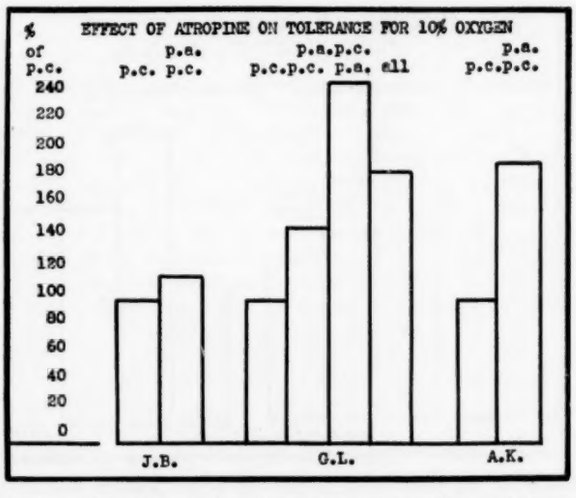


Chart 3.—The tolerance for 10 per cent oxygen after meals is represented as 100 per cent in the left hand one of each group of columns and is labeled p. c. The group of columns with the subscript G. L. represents the following: p. c., tolerance after meals = 100 per cent; p. a. p. c., atropine was given, the meal was eaten and then the test was run; p. c. p. a., the meal was eaten, atropine was given and then the test was run; all the tolerance for 10 per cent oxygen after meals and atropine regardless of the time when the drug was given.

33 per cent. Patient 2 had a very slight elevation of pressure and a normal sized heart, and from the physical examination alone it would be difficult to detect cardiac structural changes. With these data in mind, one

18. Essex, H. E.; Herrick, J. F.; Baldes, Edward J., and Mann, F. C.: Blood Flow in the Circumflex Branch of the Left Coronary Artery in the Intact Dog, Am. J. Physiol. **117**: 271-279 (Oct.) 1936. Essex, H. E.; Wegria, R. G. E.; Herrick, J. F., and Mann, F. C.: The Effect of Certain Drugs on the Coronary Blood Flow of Trained Dogs, Am. Heart J. **19**: 554-565 (May) 1940.

would suspect a much greater vasoconstrictor element in the anginal attacks of patient 2 and a greater organic element in the anginal attacks of patient 1. If this were true, one would forecast the more profound effect that the ingestion of food would have on patient 2 and a greater response from atropine after a meal. That this

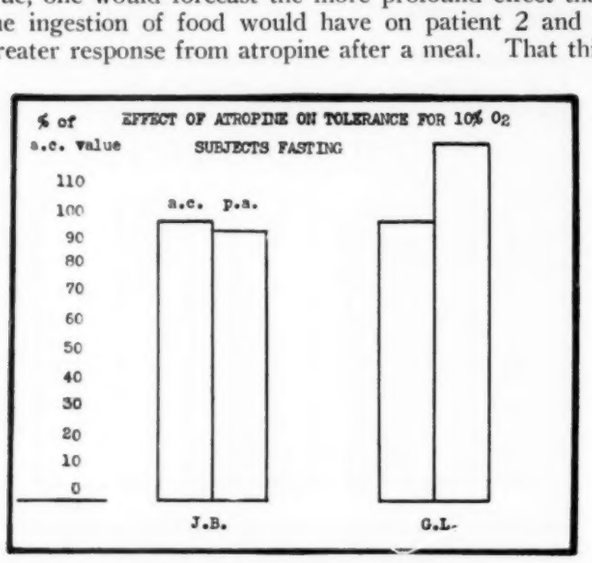


Chart 4.—The tolerance for 10 per cent oxygen before meals is represented as 100 per cent in the left hand column of each group and is labeled a. c. The tolerance for the gas mixture after atropine, and still before meals, is represented in the right hand column, labeled p. a.

was the fact was shown in table 4. The ingestion of food reduced the tolerance to 10 per cent oxygen of patient 1 by 19 per cent, of patient 2 by 40 per cent. Atropine improved the after meal tolerance for 10 per cent oxygen of patient 1 by 17 per cent, of patient 2 by 87 per cent. The remaining figures in table 4 are those from which the graphs were prepared.

In January of this year, while the work was in progress, Morrison and Swalm [19] published a report in which

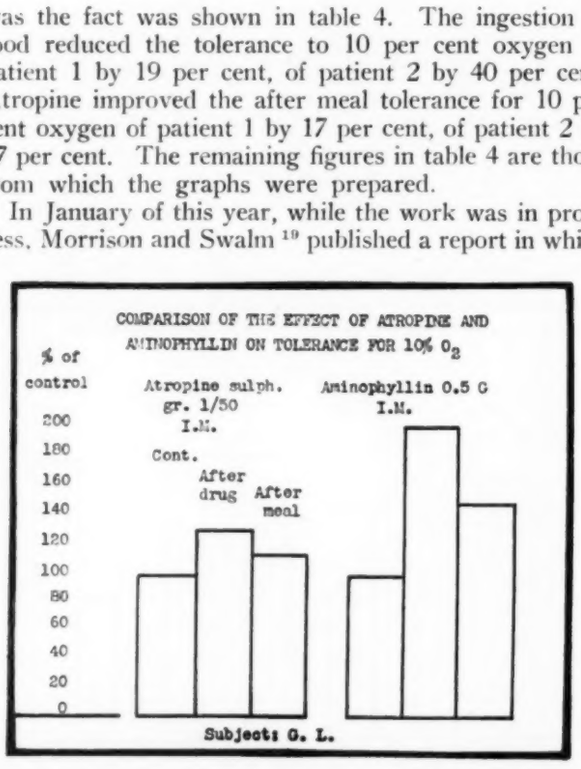


Chart 5.—The tolerance for 10 per cent oxygen before a meal is represented as 100 per cent in the left hand column of each group, labeled Cont. (control). The middle column depicts the increased tolerance for the gas twenty minutes after each drug was given. The right hand column represents the tolerance to the gas ten minutes after completion of a meal that was served immediately after the test represented in the middle column.

they approached this problem from a somewhat different angle, and we believe that our results are in every way consistent with theirs.

19. Morrison, L. M., and Swalm, W. A.: Role of the Gastrointestinal Tract in Production of Cardiac Symptoms, J. A. M. A. **114:** 217-223 (Jan. 20) 1940.

We do not need to be convinced that the xanthine bodies increase the coronary flow. Our belief in the efficiency of theobromine and theophylline has been a matter of record for several years. In addition to this, Levy [17] and his associates have already used this method to show the increase in pain time caused by the administration of these drugs. In order to compare the effect of atropine and theophylline on the same patient under the same conditions, an additional experiment was done.

We show in chart 5 that a result in the same direction may be obtained in the first instance by a vagal inhibitor and in the second instance by a coronary vasodilator. As might be expected, the active coronary vasodilator had the more marked effect. The result shown in chart 5 was the effect of a single injection of 0.5 Gm. of theophylline with ethylene diamine. When this patient had taken orally 0.6 Gm. of the drug daily for three days it was impossible to produce pain by the respiration of 10 per cent oxygen for thirteen minutes longer than the control pain time.

COMMENT

Our experiments would seem to indicate quite definitely that the coronary flow in the dog may be reduced by distention of the stomach or abdominal cavity. The results are quite constant if proper attention is paid to anesthesia and the dog is maintained in relatively good condition. In view of the fact that this reduction in flow does not occur after vagal section or after the administration of atropine, it is difficult to escape the conclusion that the reduction in flow is the result of activity of the vagus nerve. This, then, is an instance of reflex coronary vasoconstriction initiated by vagal irritation in the gastrointestinal tract. Attention has been directed to the results of other workers who have brought out evidence indicating the occurrence of a similar reflex coronary vasoconstriction initiated in the lung [10] and in the heart itself.[9] We feel that similar effects may result from irritation of the gallbladder or biliary tract, and we hope to report later on further experimental work. It would seem quite likely that such vasoconstrictor reflexes might also originate elsewhere in the viscera, but definite proof is lacking. If it is assumed that reflex coronary vasoconstriction may be the result of gastric or abdominal distention, the incidence of anginal pain following meals is explained in part.

In an effort to examine this hypothesis with patients having angina of effort, such patients were subjected to a pain-stimulating mechanism. They were made to breathe 10 per cent oxygen until the pain appeared and it was found that the time required to produce pain in a given patient was remarkably constant from test to test. This induced pain appeared much more quickly following meals, and this reduced pain time was abolished by the use of atropine. In the clinical patient the anginal attacks appear more promptly after ingestion of food. In the experimental animal, distention of the stomach was followed by a decrease in the coronary flow. In each case the effect was abolished by atropine. In the experimental animal the effect did not occur after section of the vagus.

In examining the individual patients by the method described, a fairly wide variation in the response to atropine was observed. It seemed to us that the variation of the pain time in response to atropine was in inverse proportion to the evidence of anatomic cardiac

damage. That is to say, the greater the obvious cardiac damage, the less striking is the atropine response. It is probable that the ability of a seriously damaged coronary vessel to dilate or constrict is impaired. We think that this observation indicates a vasoconstriction in the cases in which atropine gave relief. It is quite possible that the character of the atropine response by such patients may be a rough index of the character of the angina. A considerable increase in the tolerance to 10 per cent oxygen as a result of the injection of atropine by patients subjected to this procedure would lead us to suspect that the anginal attack had a large vasoconstrictor element. Conversely, a small atropine response would indicate that the angina was largely due to anatomic changes in the vessel.

CONCLUSIONS

Distention of the dog's stomach under light anesthesia or no anesthesia at all produces coronary vasoconstriction through a vagovagal reflex. This reflex with its resultant coronary constriction may be abolished by atropine or by vagal section.

Anginous patients who were made to breathe 10 per cent oxygen developed anginal pain much more quickly following meals. This reduced pain time was abolished by the use of atropine and, in two of the three patients, atropine caused the after meal pain time to exceed the control pain time.

104 South Michigan Avenue.

ABSTRACT OF DISCUSSION

DR. LESTER M. MORRISON, Philadelphia: Drs. Gilbert, Fenn and LeRoy have shown the relationship of intragastric gassy distention on the coronary arteries. It is gratifying to find their work in complete agreement with my experimental and clinical studies reported in THE JOURNAL, January 20. At that time Dr. Swalm and I recorded the effect and relationship of intragastric and intra-esophageal gassy distention on the coronary arteries and angina pectoris in man for the first time and showed their direct relationship clinically through the vagus arc. When we first conducted our experiments in 1935 it took Dr. Peckham and myself some six months to devise a safe apparatus, because of the danger of inducing a fatal attack in the cardiac cases. Indeed, when I distended the stomach to 100 mm. of mercury pressure one of the patients developed a cardiac standstill and fell unconscious. If we had not constructed our apparatus so that I could relieve the intragastric pressure immediately, I feel certain that the patient would have died then and there. It is a tribute to the skill and ingenuity of Drs. Gilbert, Fenn and LeRoy that their method of approach was so eminently successful. The variability of the time-pain in each of the cases presented indicates the difference in vagal pattern sensitivity in different patients. This calls for saturation dosages of atropine or belladonna for therapeutic effectiveness. Dr. Fenn told me that the experimental meals were given at the lunch hour. Even more striking results may have been obtained following the heavy evening meal, which is a much heavier load placed on the stomach and the vagus nerve mechanism. The clinical inferences of this presentation are significant. In angina pectoris and coronary artery disturbances the necessity is for small, frequent meals, proper diet, antispasmodics, sedatives and xanthine derivatives. The diet should be relatively bland, easily digested and free from all gas-forming foods. Light meals should always be eaten slowly and chewed thoroughly. Active physical exercise or excitement after meals is always hazardous in these cases and is to be avoided at all times. The bowels should function normally and daily. Flatulence is to be avoided like the plague and can be combated with soothing gastric and bowel demulcents, antacid powders, carminatives and absorbents.

DR. CHARLES W. GREENE, Stanford University, Calif.: It is reassuring to find that clinicians are laying more and more emphasis on the part played by physiologic processes in the origin and course of cardiac disorders. The foundation of the nutritive control of the myocardium lies in intimate regulation of the coronary blood flow. It is the details of this regulation that are being uncovered by the numerous coronary researches of the last two decades. Sensory events in every part of the body produce autonomic reflexes directly affecting the rate and volume of the coronary blood flow. It matters not what associated reactions may simultaneously occur. Dr. Gilbert and his colleagues have added the demonstration of the part played by visceral pressure stimulation. A fact not generally known is that the milder and usual functional coronary reflexes take the form of coronary dilatations. Reflex coronary constrictions occur in the normal animal only in response to more vigorous sensory stimulation. If, as is often the case, the constrictor reflex apparatus is hypersensitive or overdeveloped, coronary constrictions are more frequent, even dominant, and may be profound enough to induce varying degrees of myocardial ischemia. The authors have used the two reliable and standard experimental methods applicable to dogs, the coronary sinus method and the electrical stromuhr technic. Each method is difficult but each yields data which supplement the other. The addition of direct experiments on anginal patients is unique. The method arrives at the cardiac crisis sooner. The reported results are positive and definite. Let me emphasize that reflex coronary reactions are almost always associated with cardiac accelerations, not slowing or inhibitions as is too often inferred. This is the explanation of the coronary dilatation as the normal and standard reaction. The coronary dilatation supplies more oxygen when the myocardial consumption is greater. One can appreciate the upset of this physiologic balance when the coronary arteries are reflexly constricted, thus actively reducing the coronary flow. It is equally tragic if the coronaries of the patient are sclerotic or have lost coronary resilience and cannot respond to the associated coronary dilator reflexes when the heart is doing increased work. The authors are to be congratulated for establishing that visceral pressures induce reflex coronary constrictions that hasten anginal attacks.

DR. HEYMAN R. MILLER, New York: These studies touch on two major problems: The first deals with the question Does anoxemia with a resultant myocardial ischemia produce anginal pain? Does anginal pain associated with abdominal distention depend on anoxemia? The other major problem is unrelated to anoxemia and has to do with the transmission of afferent impulses from the abdomen and its viscera to those spinal cord segments at which referred cardiac pain is mediated. Afferent abdominal stimuli are probably also registered in the cardiac apparatus by means of axon reflexes, without passing through the spinal cord. May I ask whether it is not possible to have an anoxemia, a diminished oxygen content in the circulation, and yet an oxygen content in the heart muscle above the critical level requisite for the induction of pain? I put the question because the heart with its special arrangement of autonomic supplies seems able to receive more rather than less blood in the presence of an emergency like asphyxia; the coronary vessels probably dilate. Moreover, in certain experimental and clinical situations the heart, despite low oxygen content of the blood, can remain free of pain. While intense pain will appear at the moment of tightening a ligature around a coronary vessel, shortly thereafter, and despite continued anoxemia of the heart muscle, pain may subside or disappear. Again, at the onset of an acute coronary thrombosis, pain is often intense yet within a few hours cardiac pain may be greatly diminished or absent even though the infarcted segment of myocardium is still deprived of considerable oxygen. These observations are offered not as complete detractions of the general concept that anoxemia may lead to cardiac pain but rather to suggest that factors other than anoxemia alone are at work. The observations of Dr. Greene and his co-workers indicate that a reflex may operate between abdominal viscera and the coronary circulation. I venture to believe, however, that such a reflex may influence coronary flow independent of the mechanism of pain transmission.

THE TREATMENT OF ANURIA DUE TO SULFAPYRIDINE CALCULI

JOSEPH F. SADUSK JR., M.D.
LEVIN WATERS, M.D.
AND
DWIGHT WILSON, M.D.
NEW HAVEN, CONN.

The symptom complex of hematuria, abdominal pain, and nitrogen retention as a manifestation of sulfapyridine therapy was first described by Southworth and Cooke,[1] although the occurrence of hematuria had been previously noted.[2]

Animal experiments by Antopol and Robinson,[3] Gross, Cooper and Lewis [4] and Toomey [5] early revealed the pathologic changes in the urinary tract of rats, rabbits and monkeys receiving sulfapyridine. Since then, Antopol and Robinson [6] and Toomey, Reichle and Takacs [7] have studied these changes in great detail. Briefly they are as follows: in the kidneys, striking dilatation of the glomerular spaces and tubules; thickening of the basement membranes of the glomerular tufts with changes in the shape of the cells of the capsular epithelium; in the collecting tubules, débris and spaces, apparently the lodging place of crystals of the precipitated drug; in the pelves and ureters, concretions, with denuding of the epithelium, clotted blood, mucosal hemorrhages and marked edema.

The seriousness of this manifestation of sulfapyridine treatment in man became evident with the report of a death from total anuria by Tsao and his co-workers.[8] This report was of particular interest in that the finding of complete ureteral obstruction due to concretions blocking both ureterovesical orifices was described. These authors suggested the use of cystoscopic treatment, believing that their patient would have survived if this procedure had been carried out.

Recently Carroll, Shea and Pike [9] have successfully treated by cystoscopy a patient who had complete anuria due to sulfapyridine calculi and have recorded the finding of ureteral obstruction by calculi at the ureterovesical orifices.

Our purpose in the present contribution is to offer additional evidence (1) that complete anuria due to sulfapyridine may be caused by ureteral obstruction and (2) that this condition can be treated effectively by means of cystoscopy. The renal pathologic changes in one instance of acute sulfapyridine anuria will be described.

From the Departments of Internal Medicine, Pathology and Surgery of the Yale University School of Medicine and the New Haven Hospital.

1. Southworth, Hamilton, and Cooke, Crispin: Hematuria, Abdominal Pain and Nitrogen Retention Associated with Sulfapyridine, J. A. M. A. **112**: 1820 (May 6) 1939.

2. Lawrence, E. A.: Recent Advances in the Treatment of Pneumonia, International Review of Recent Advances in Medicine **3**: 45 (Jan.) 1939. Hanssen, Per: Treatment of Lobar Pneumonia with M. & B. 693, Lancet **1**: 61 (Jan. 7) 1939. Graham, Duncan; Warner, W. P.; Dauphinee, J. A., and Dickson, R. C.: The Treatment of Pneumococcal Pneumonia with Dagenan (M. & B. 693), Canad. M. A. J. **40**: 325 (April) 1939.

3. Antopol, William, and Robinson, Harry: Urolithiasis and Renal Pathology After Oral Administration of 2(Sulfanilylamino) Pyridine (Sulfapyridine), Proc. Soc. Exper. Biol. & Med. **40**: 428 (March) 1939.

4. Gross, Paul; Cooper, F. B., and Lewis, Marion: Urinary Concretions Caused by Sulfapyridine, Proc. Soc. Exper. Biol. & Med. **40**: 448 (March) 1939; Urinary Calculi Caused by Sulfapyridine, Urol. & Cutan. Rev. **43**: 299 (May) 1939. Gross, Paul; Cooper, F. B., and Lewis, Marion: The Fate of Urinary Calculi Caused by the Administration of Sulfapyridine, ibid. **43**: 439 (July) 1939.

5. Toomey, J. A.: Urinary Concretions and Sulfapyridine, J. A. M. A. **113**: 250 (July 15) 1939.

6. Antopol, William, and Robinson, Harry: Pathologic and Histologic Changes Following Oral Administration of Sulfapyridine, with a Short Note on Sulfapyridine, Arch. Path. **29**: 67 (Jan.) 1940.

7. Toomey, J. A.; Reichle, H. S., and Takacs, W. S.: Effects on Monkeys of Sulfapyridine in Doses Comparable with Those Used for Infants, J. Pediat. **16**: 179 (Feb.) 1940.

8. Tsao, Y. F.; McCracken, Mary E.; Chen, Ji; Kuo, P. T., and Dale, C. L.: Renal Complications in Sulfapyridine Therapy, J. A. M. A. **113**: 1316 (Sept. 30) 1939.

9. Carroll, Grayson; Shea, John, and Pike, George: Complete Anuria Due to Crystalline Concretions Following the Use of Sulfapyridine in Pneumonia, J. A. M. A. **114**: 411 (Feb. 3) 1940.

REPORT OF CASES

CASE 1.—*History.*—A man aged 35, Italian, a laborer, was admitted on Feb. 3, 1940, to the Neurosurgical Service of the New Haven Hospital following a traumatic injury to the head with penetration of a foreign body into the right frontal region of the brain. Little was known of his past history other than that he had enjoyed good health up to the time of the accident.

On admission the patient was unconscious, breathed stertorously and did not respond to stimuli. The temperature was 100.2 F., pulse 88 and respiratory rate 48. The blood pressure was 190 systolic, 120 diastolic but shortly after admission fell to 110 systolic, 80 diastolic. Examination revealed a deep laceration of the right frontal region in which was embedded a foreign object. Shortly after admission the patient fell into shock but after operative removal of the foreign body and blood transfusion he rallied and his condition seemed quite satisfactory.

Fig. 1 (case 1).—Retrograde pyelogram before lavage of kidney pelves.

Following operation the administration of sulfapyridine was commenced as a prophylactic measure but, despite this, infection of the operative wound set in within forty-eight hours and cultures of the pus yielded a growth of hemolytic Staphylococcus albus and aureus. Essential details of the patient's course are outlined in table 1. On the first day he received 3 Gm. of sulfapyridine, the first 2 Gm. of which was administered subcutaneously in 750 cc. of saline solution and 750 cc. of 5 per cent dextrose. All subsequent sulfapyridine was given by mouth in the amount of 1 Gm. every four hours until February 6. On this date because of a rather low blood level of free sulfapyridine the dosage was increased to 1 Gm. every three hours.

At noon on February 7 the patient complained of pain in the flanks. That night the urine was found to be of a dark amber color and to contain about 25 red cells per high power field in an uncentrifuged specimen. Sulfapyridine was immediately discontinued and fluids were forced as much as possible under the circumstances of the accompanying neurologic condition.

The following day the patient was irritable but responded well to stimuli. Respirations were rapid. The left retinal fundus was normal in appearance. The lungs were clear throughout, and examination of the cardiovascular system revealed no abnormalities. The abdomen was greatly distended and tym-

Fig. 2 (case 1).—Retrograde pyelogram after lavage of kidney pelves.

panitic. Palpation over both costovertebral angles showed definite tenderness. There was no peripheral edema. Little fluid had been taken by mouth. Consequently fluids were given parenterally in a total amount of 3,100 cc. as follows: 300 cc. transfusion of blood, 1,000 cc. of 10 per cent dextrose solution and 300 cc. of physiologic solution of sodium chloride intra-

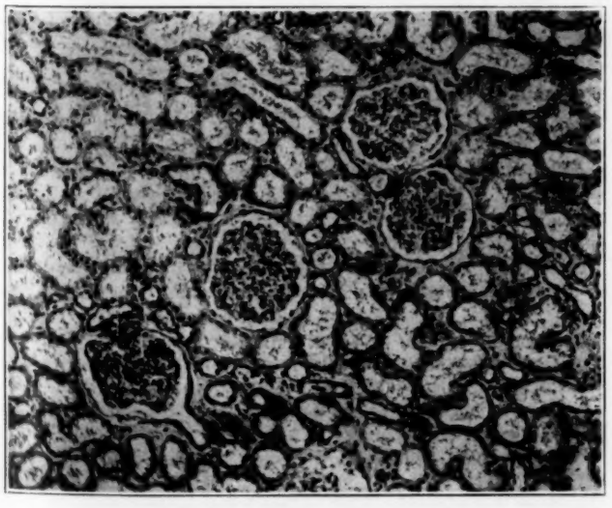


Fig. 3 (case 1).—Section of renal cortex showing dilatation of tubules and glomerular spaces. Reduced from a photomicrograph with a magnification of 100 diameters.

venously, and 1,000 cc. of physiologic solution of sodium chloride and 500 cc. of 5 per cent dextrose solution by hypodermoclysis.

During the remainder of the day the patient complained rather bitterly of persistent pain in the flanks and difficulty in voiding. At 4:30 p. m. he passed 60 cc. of grossly bloody urine, his last voided specimen.

Following this there was complete anuria during the next twenty-four hours, despite intravenous injection of physiologic solution of sodium chloride and 50 per cent dextrose. The possibility of sulfapyridine calculi blocking the ureters was considered and it was decided that cystoscopy was indicated, since the patient's nonprotein nitrogen was now 76 mg. per hundred cubic centimeters.

A No. 24 French cystoscope was passed with ease. Approximately 50 cc. of pinkish cloudy amber urine was found in the bladder and showed the characteristics detailed in table 2. In it were many long slender crystals and large flat ones which were jagged and irregular. The bladder capacity was less than 100 cc. The mucous membrane was injected and a few small blood clots were present. The ureteral orifices were inflamed and a small blood clot was seen protruding from the left meatus. Neither ureteral orifice passed any urine. Attempts to pass the ureteral catheters met obstruction on both sides at a depth of 1 cm. The catheters were then withdrawn and after the passage of No. 5 filiform tipped bougies, No. 7 French ureteral bougies were passed to the renal pelvis on both sides. Following withdrawal of these, a sharp, multipointed concretion was seen extruding from the right ureteral orifice. This was easily dislodged. Each ureteral orifice was now seen to produce bloody urine and on catheterization yielded urine as described in table 2.

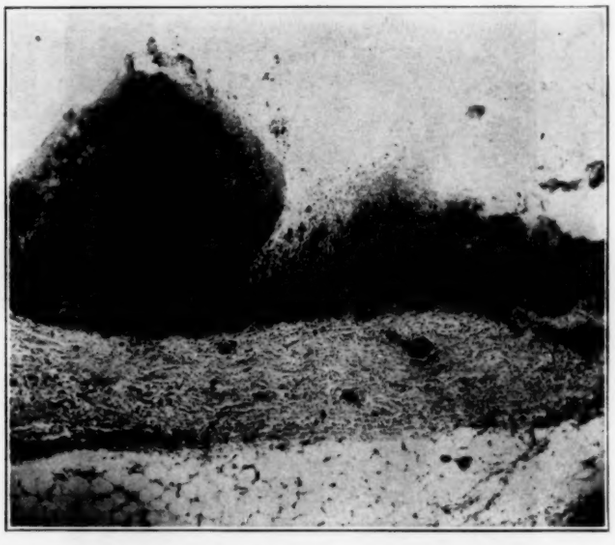


Fig. 4 (case 1).—Section of renal pelvis showing the loss of epithelium and the massive hemorrhagic infiltration of the lamina propria mucosae. Note also the congestion of the submucosal vessels and the cellular infiltration of this layer. Reduced from a photomicrograph with magnification of 40 diameters.

An x-ray film of the abdomen was rather unsatisfactory because of intestinal distention, but no evidence of radiopaque renal or ureteral calculi was found. A retrograde pyelogram (fig. 1) revealed poorly outlined renal pelves with mottling and hazy outlines. Both catheters were now repeatedly washed out with warm sterile water for a period of about thirty-five minutes. At the end of this period the urine draining from the left catheter was fairly clear while that draining from the right catheter remained blood tinged. A retrograde pyelogram (fig. 2) now revealed more sharply outlined kidney pelves. The ureteral catheters were allowed to remain in place, the left producing from 50 to 60 drops a minute and the right from 30 to 40 drops a minute.

The patient was then returned to the ward and during the next two hours continued to excrete urine satisfactorily from both catheters, at the end of which time he pulled the catheters out of place. Shortly after this, 1,000 cc. of 5 per cent dextrose solution was given slowly by the intravenous route. Approximately thirty minutes after the infusion was finished the patient lapsed into coma and, despite supportive measures, died of respiratory failure, presumably due to cerebral edema and medullary compression.

Pathologic Examination.—Autopsy was limited to an examination of the kidneys and the upper portions of the ureters. Grossly the kidneys were enlarged, the right weighing 230 Gm. and the left 215 Gm. The measurements for the right were 12 by 7 by 5 cm. and for the left 12 by 6 by 4.5 cm. Both

Fig. 5 (case 2).—Retrograde pyelogram before lavage of kidney pelves.

organs were light brown and quite soft. Their capsules stripped with ease, leaving a smooth surface on which there was no evidence of potential hemorrhages. On longitudinal section the

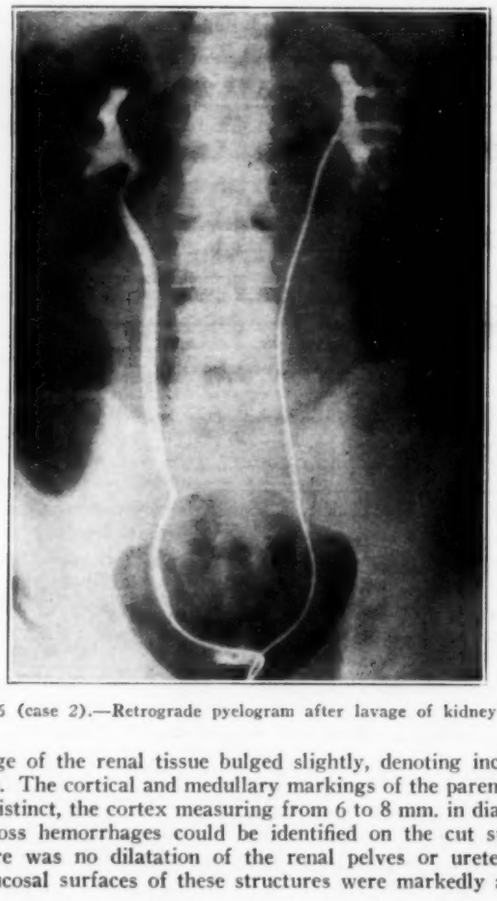


Fig. 6 (case 2).—Retrograde pyelogram after lavage of kidney pelves.

cut edge of the renal tissue bulged slightly, denoting increased tension. The cortical and medullary markings of the parenchyma were distinct, the cortex measuring from 6 to 8 mm. in diameter. No gross hemorrhages could be identified on the cut surface.

There was no dilatation of the renal pelves or ureters but the mucosal surfaces of these structures were markedly altered in appearance. Much red-brown clotted blood, rather granular in consistency, filled the calices and was adherent to large areas of the pelvic and ureteral mucosa. Where there was no actual clot the pelvis and ureteral mucosal surfaces were hemorrhagic, being raised here and there into small bleblike masses filled with blood. The walls of the pelves and ureters were markedly edematous. No concretions were present, but in the calices, mixed with the clotted blood, were found small amorphous masses of a light red-brown material which was gritty to palpation. Under the microscope numerous needle shaped and sheaflike crystals were identified. Chemical analysis [10] of this material revealed the presence of 45 per cent acetylated sulfapyridine and 6 per cent free sulfapyridine.

Microscopically the most striking change in the kidney proper was the great dilatation of the convoluted and collecting tubules and of the glomerular spaces. A considerable amount of eosinophilic granular material was observed in the convoluted tubules. In a few of the collecting tubules, basophilic amorphous masses were found but no other concretions or crystals were present. The glomerular changes were interesting. In addition to the distention of Bowman's capsule the tufts were enlarged with greatly congested capillaries and a much vacuolated intercapillary basement membrane. In numerous tufts the red blood cells within the capillaries were apparently fused or conglu-

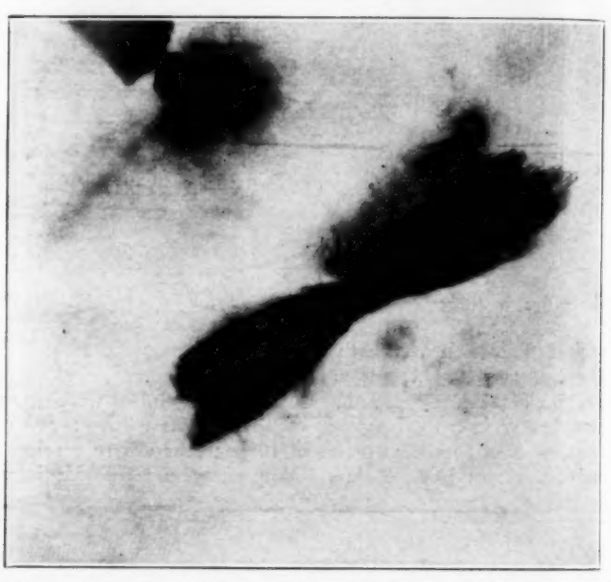


Fig. 7 (case 2).—Sheaf of crystals of acetyl sulfapyridine recovered from the ureteral calculi; × 200.

tinated to form homogenous eosinophilic masses. Neither necroses of the glomerular tufts nor intracapsular hemorrhages were found. The epithelium of the renal tubules was intact throughout. Focal areas of capillary congestion were frequent and there was much interstitial edema.

The renal pelves showed for the most part absence or necrosis of their transitional epithelium. The lamina propria mucosae was edematous and contained large hemorrhagic extravasations, some of which resulted in the nodular masses noted grossly. Numerous lymphocytes and polymorphonuclear leukocytes were present. Similar hemorrhagic extravasations and cellular accumulations extended in focal zones through the submucosa well up into the medullary renal tissue.

Microscopically the ureters showed extensive mucosal hemorrhages, great edema of all the coats of the wall and an abundant lymphocytic and polymorphonuclear cellular infiltration.

CASE 2.—A man aged 39, Italian, a laborer, was first admitted for therapy to the Medical Service of the New Haven Hospital on Dec. 11, 1939, with a subacute gonorrheal urethritis, prostatitis and arthritis. Some degree of improvement occurred on sulfanilamide therapy, but the patient left the hospital against advice on Dec. 26, 1939.

10. Chemical analyses in this report were performed by Miss Anne Seymour.

Eight days after discharge the patient again had a urethral discharge, which was shortly followed by pain and swelling of both ankles and the right knee. He was readmitted on Feb. 7, 1940, with an arthritis of both ankles and the right knee, the latter being quickly followed by spread to the left knee. His temperature was 102 F. and blood pressure 120 systolic, 80 diastolic. The leukocyte count was 11,300. Examination of the urine revealed no albumin or red cells, but from 1 to 2 leukocytes per high power field were present. X-ray examination of the ankles and right knee revealed changes consistent with a subacute infectious arthritis.

After a preliminary period of observation, sulfathiazole therapy was begun, the patient receiving an initial dose of 4 Gm. followed by 1 Gm. every four hours. No response in temperature or symptoms was obtained and after six days of therapy sulfathiazole was discontinued. Specific details as to the laboratory data are contained in table 4.

Twenty-four hours after the discontinuance of sulfathiazole the blood concentration of the drug had fallen to a trace, and eight hours after this determination sulfapyridine therapy was begun, the patient receiving an initial dose of 4 Gm. and then 1 Gm. every four hours. On the third day of sulfapyridine therapy (February 19) it was noted that 55 per cent of the drug in the blood was acetylated, but in view of a normal urine, a nonprotein nitrogen of 27 and a satisfactory urine output it seemed advisable to continue sulfapyridine therapy. Late that night the patient complained of lower abdominal pain but nothing was found on physical examination except abdominal distention.

TABLE 1.—*Data in Case 1*

Date	Sulfapyridine Administered. Gm.	Fluid Intake, Cc.	Urinary Output, Cc.	Sulfapyridine Blood Concentration: Free, Mg. %	Total, Mg. %	Acetyl., %	Nonprotein Nitrogen, Mg. %	CO_2, Vol. %	Chloride, mEq.
Feb. 3	3.0	1,500	400	...	....	..	..	....	....
4	6.0	2,000	600	...	....	..	..	....	....
5	6.0	2,000	650	2.4	....	..	..	....	....
6	8.0	960	350	3.3	....	..	..	....	....
7	6.0	4,200	425	3.1	....	..	..	....	....
8	...	4,100	135	...	....	..	70	49.0	99.4
9	...	2,800	0	2.2	15.2	85	76	44.9	97.0

Intake and output levels on twenty-four hour specimen from 7 a. m. to 7 a. m. The fluid intake includes fluids given parenterally.

At 4 o'clock the following morning (February 20) the patient passed a dark smoky urine containing innumerable red cells, 3 plus albumin and numerous crystals, among which were a type resembling bound sheaves of wheat. This specimen contained 92.4 mg. per hundred cubic centimeters of free sulfapyridine and 235 mg. total sulfapyridine (61 per cent acetylated). From this point on the patient had an essentially complete anuria and now complained of rather severe pain definitely localized over the suprapubic area and the costovertebral angles. The nonprotein nitrogen had risen to 35 mg. per hundred cubic centimeters and total blood sulfapyridine to 13.7 mg., 57 per cent of which was acetylated. There was a leukocytosis of 22,200, 85 per cent of the cells being of the granulocytic series.

Sulfapyridine was immediately discontinued and fluid forced both orally and parenterally, the patient receiving 1,000 cc. of 10 per cent dextrose intravenously and 3,250 cc. of physiologic solution of sodium chloride and 750 cc. of 5 per cent dextrose by hypodermoclysis. During the course of the day the patient complained bitterly of pain in the flanks and lower part of the abdomen. There was costovertebral tenderness, more marked on the right.

Except for 5 cc. of bloody urine passed at 5 a. m. February 21, which had essentially the same characteristics as the last specimen passed on February 20, no further urine was produced. By the morning of February 21 he had become drowsy and lethargic. The nonprotein nitrogen had risen to 45 mg. per hundred cubic centimeters and the total blood sulfapyridine to 15 mg., 67 per cent of which was in the acetylated form. At 3:30 that afternoon, after anuria for thirty-six hours, cystoscopy was performed.

A No. 24 French cystoscope was passed without difficulty, a slightly grating sensation being noted. About 20 cc. of grossly bloody urine was found in the bladder. The bladder capacity was 200 cc. The bladder mucous membrane was fairly normal except for moderate inflammation in the region of the trigon. There were numerous mucous shreds and yellowish concretions in the base of the bladder. Neither ureteral orifice produced any urine. The right ureteral orifice was swollen, edematous and dusky red, and humped up on a mount about 1 cm. in diameter. Protruding from the ureteral orifice could be seen a large irregular concretion completely filling the meatus. The left ureteral orifice was similarly involved but less edematous and was also completely filled with a calculus. No. 5 French ureteral catheters were then passed. There was moderate obstruction for a distance of about 2 cm. from the meatus. Beyond this point they passed without difficulty to the renal pelves, urine dropping from the left ureteral catheter quite steadily, but more slowly on the right. The right ureteral catheter was then withdrawn momentarily and a most remarkable sight was seen. Pouring from the right ureteral orifice was a thick sludge, probably sulfapyridine "sand," quite similar in appearance to the pouring of a thick semisolid cement mixture. After this material was discharged the catheter was reinserted and ureteral specimens were taken for examinations which are summarized in table 3. An x-ray film of the abdomen revealed no radiopaque calculi present. A retrograde pyelogram (fig. 5) revealed a dilatation of the right ureter. The renal pelves were fairly normal though rather mottled in appearance, this being especially true of the right kidney pelvis. The catheters were then thoroughly lavaged with warm distilled water and the pyelogram was repeated (fig. 6), showing better filled pelves with clearer outlines.

TABLE 2.—*Characteristics of Urine from Bladder, Right Ureteral Catheter and Left Ureteral Catheter Obtained at Cystoscopy in Case 1*

	Bladder	Right Kidney	Left Kidney
Appearance	Pinkish, cloudy amber	Grossly bloody	Cloudy amber
Reaction	Acid	Acid	Acid
Albumin	+	+++	+
Sediment (centrifuged)			
Red blood cells	Innumerable	Innumerable	50 per high power field
White blood cells	Occasional	None	None
Casts	None	None	None
Epithelial cells	Moderate number	None	None
Sulfapyridine concentration			
Free	70 mg. per 100 cc.	65 mg. per 100 cc.	90 mg. per 100 cc.
Total	325 mg. per 100 cc.	265 mg. per 100 cc.	395 mg. per 100 cc.
Acetylation	78 per cent	76 per cent	77 per cent
Culture	Sterile		

TABLE 3.—*Characteristics of Urine from Bladder, Right Ureteral Catheter and Left Ureteral Catheter Obtained at Cystoscopy in Case 2*

	Bladder	Right Kidney	Left Kidney
Appearance	Grossly bloody	Blood tinged	Cloudy amber
Reaction	Neutral	Acid	Acid
Albumin	+++	+	Trace
Sediment (centrifuged)			
R. B. C.	Innumerable	Innumerable	100 per h. p. f.
W. B. C.	25 per h. p. f.	Occasional	Occasional
Casts	None	None	None
Sulfapyridine Conc.			
Free	.....	80.0 mg. per 100 cc.	47.5 mg. per 100 cc.
Total	.....	210.0 mg. per 100 cc.	145.0 mg. per 100 cc.
Acetylation	.....	62%	67%
Culture	.....	Sterile	Sterile

Phenolsulfonphthalein was injected intravenously, appearance times of the drug being four and one-half and three minutes respectively on the left and right sides. Excretion on the left side in fifteen minutes was 2.5 per cent, while on the right side

it was approximately 10 per cent, the latter figure being unreliable owing to the presence of blood. A number of small stones were then washed out of the bladder and preserved. They were yellowish white, irregularly spherical and easily crushed. Microscopically they were made up for the most part of groups of crystals resembling bound sheaves of wheat (fig. 7) together with a number of long slender needles (probably from the breaking up of the sheaves) and crystals of nonacetylated sulfapyridine. Chemical analysis of these calculi showed that they contained 55 per cent of acetylated sulfapyridine and 7 per cent of free sulfapyridine.

The ureteral catheters were allowed to remain in place for the next twelve hours. Urine dropped steadily from each ureteral catheter, and from time to time the patient voided spontaneously around the catheters. During this period the left catheter yielded 255 cc. of urine containing 35 mg. per hundred cubic centimeters of free sulfapyridine and 110 mg. of total sulfapyridine (68 per cent acetylation), the right catheter 370 cc. of urine containing 37.5 mg. per hundred cubic centimeters of free sulfapyridine and 115 mg. of total sulfapyridine (67 per cent acetylation).

Following removal of the catheters the patient continued to pass considerable quantities of a dark smoky urine containing red cells, albumin, mucous shreds and many very small calculi, which on microscopic examination showed again the presence of large jagged crystals, apparently broken up acetylated sulfapyridine crystals. He continued to pass similar urine until the night of February 22, following which the urine assumed a slightly cloudy, yellow appearance. The urine continued to clear, the albumin disappeared and only rare red and white cells were found. At the time of discharge the urine was entirely negative save for an occasional leukocyte. Casts were never found in the urine at any time. Phenolsulfonphthalein excretion on February 26 was 63 per cent in two hours. An intravenous pyelogram revealed normal kidney pelves and normal ureters, the dilatation of the right ureter previously observed being no longer present.

The patient was discharged on March 12, 1940, in good condition with temperature normal, arthritis practically subsided and normal urinary status.

TABLE 4.—*Data in Case 2*

Date	Dosage of Sulfathiazole, Gm.	Dosage of Sulfapyridine, Gm.	Fluid Intake 24 Hr., Cc.	Urinary Output, Cc.	Leukocytes in Blood	Sulfathiazole Blood Concentration: Free, Mg. per 100 Cc.	Sulfathiazole Blood Concentration: Total, Mg. per 100 Cc.	Sulfathiazole Blood Concentration: Acetylation, %	Sulfapyridine Blood Concentration: Free, Mg. per 100 Cc.	Sulfapyridine Blood Concentration: Total, Mg. per 100 Cc.	Sulfapyridine Blood Concentration: Acetylation, %	Nonprotein Nitrogen, Mg. per 100 Cc.	Urine: Albumin	Urine: R. B. C. per H. P. F.	Urine: W. B. C. per H. P. F.
Feb. 10	6.0	...	.....	.....	9,600	...	...	..	...	...	..	..	..	..	..
11	6.0	...	.....	.....	9,500	...	...	..	...	...	..	..	0	0	..
12	6.0	...	.....	.....	10,100	2.9	3.8	23	...	...	..	..	0	0	..
13	6.0	...	2,800	1,250	10,200	3.8	4.5	16	...	...	..	..	0	0	..
14	6.0	...	3,700	1,550	12,200	3.1	3.6	14	...	...	..	28	0	0	..
15	6.0	...	3,300	1,900	7,700	3.1	4.0	23	...	...	..	..	0	0	..
16	1.0	...	3,200	1,760	7,400	2.6	3.5	26	...	...	..	..	0	0	..
17	...	7.0	3,770	3,000	8,800	tr.	tr.	..	...	...	..	..	0	0	..
18	...	6.0	3,100	1,750	7,800	...	...	..	...	...	..	..	0	0	..
19	...	6.0	3,050	2,850	7,100	...	...	..	3.2	7.2	55	27	0	0	..
20	...	1.0	6,600	5	22,200	...	...	..	5.9	13.7	57	35	+++	100	5
21	...	...	2,450	939	18,700	...	...	..	4.9	15.0	67	45	++	100	5
22	...	...	2,700	2,195	12,300	...	...	..	1.9	7.4	74	..	+	10	5
23	...	...	4,450	2,420	10,600	...	...	..	0.7	3.8	82	39	0	rare	3
24	...	...	3,100	2,450	15,800	...	...	..	tr.	1.0	..	39	..	..	..
25	...	...	5,770	1,550	.....	...	...	..	tr.	tr.	..	..	..	..	..
26	...	...	2,850	1,275	12,000	...	...	..	...	...	..	34	..	..	..
27	...	...	4,050	1,100	.....	...	...	..	...	...	..	..	0	rare	rare
28	...	...	3,945	1,650	.....	...	...	..	...	...	..	30	..	..	..

Intake and output levels on twenty-four hour specimens from 7 a. m. to 7 a. m. The fluid intake includes fluids given parenterally. Medication charted for twenty-four hours, 4 a. m. to 4 a. m.

The conditions under which sulfapyridine hematuria and concretions develop are still not clear. Acidity of the urine has frequently been suggested as a factor and the simultaneous administration of sodium bicarbonate with the sulfapyridine to alkalize the urine has been advised. That this procedure is of little value has been demonstrated by clinical [8] and experimental [7] observations. In addition there has been observed in this hospital an instance of sulfapyridine hematuria developing in a patient receiving adequate amounts of sodium bicarbonate, whose urine was alkaline at the time of hematuria. Haviland and Bratton [13] have shown that the solubility of acetyl sulfapyridine in urine remains essentially the same for a range of p_H 3.3-7.4, and that the solubility at p_H 7.9 is not enough to be of therapeutic advantage.

COMMENT

In both cases there remains no doubt that the anuria was due to concretions blocking the ureterovesical orifices, thus confirming the observations of Tsao and his co-workers [8] and Carroll, Shea and Pike.[9]

That concretions may exist without blocking the ureters has been demonstrated by Plummer and McLellan.[11] Under these circumstances treatment of sulfapyridine hematuria by means of forced fluids alone seems ample, since data [12] have been offered to suggest that the concretions may be redissolved or washed out.

If, however, complete anuria is present or if the possibility of a unilateral obstruction is evident, cystoscopy should be done without delay to determine whether or not urine is being passed from the ureteral orifices. If not, catheterization of the ureter, a filiform tipped bougie being used if necessary, should be carried out and the kidney pelvis and ureter thoroughly lavaged with warm distilled water until the urine drips from the catheter and retrograde pyelograms reveal a clearly outlined upper urinary tract.

It is perhaps preferable to leave the ureteral catheters in place for the next twelve hours, though this may not be absolutely necessary. From time to time the catheters should be irrigated with warm saline solution and after their withdrawal fluids should be continually forced with close observation of the urinary output for the next forty-eight hours.

11. Plummer, Norman, and McLellan, Frederick: The Production of Sulfapyridine Renal Calculi in Man Following Administration of Sulfapyridine, J. A. M. A. **114**: 943 (March 16) 1940.
12. Antopol and Robinson.[6] Plummer and McLellan.[11]
13. Personal communication to the authors from Dr. James W. Haviland and Dr. A. Calvin Bratton, Johns Hopkins University, Baltimore.

Another factor suggested and one which has seemed most likely, has been that of a low urinary output. The validity of this explanation, however, must be seriously challenged in the light of recent experience. In case 2 the urinary output would appear to have been quite adequate and, furthermore, instances have been observed in this clinic in which the urinary output has been far less without the development of hematuria or other associated symptoms. Moreover, Toomey, Reichle and Takacs [7] have demonstrated that the administration of large quantities of fluid to the Macaca mulatta monkey has not prevented either the formation of stones or the development of pathologic changes in the urinary tract.

It is of interest that, in the cases presented in this report, acetylation of sulfapyridine both in the blood and in the urine was abnormally high. This has been true, in general, of the cases of sulfapyridine hematuria observed in this hospital,[14] but it must be pointed out again that similiar degrees of acetylation have been observed in cases which have not exhibited any sign of urinary abnormality.

Toomey and his co-workers [7] have made the interesting observation that the sodium salt of sulfapyridine, when used in comparable doses, is more apt to produce toxic urinary symptoms than is sulfapyridine. The significance of this observation is not exactly clear at the present time.

In general, the pathologic changes in case 1 were entirely in accord with those found experimentally in monkeys by Antopol and Robinson.[6] They consisted essentially of great tubular and capsular dilatation, marked congestion and vacuolization within the glomerular tufts, and an acute hemorrhagic pyelo-ureteritis extending into the adjacent renal medullary tissue. A similar pathologic description in man has been given by Tsao and his associates,[8] and Plummer and McLellan [11] mention petechial hemorrhages in the pelvis of the kidney.

On the other hand, while Stryker [15] found dilatation of the tubules and capsular spaces in the kidneys of a patient, he observed no changes in the mucosal surfaces of the urinary tract. He believes that certain basophilic masses found plugging the tubules are responsible for the tubular dilatation and represent crystals of precipitated drug. A few such masses were found in the collecting tubules of the kidneys described in the present case. Since the tissues were fixed in Zenker-acetic or in solution of formaldehyde and even washed during the staining process, it is possible that many more of these bodies were originally present. However, Strong [16] has shown in recent animal experiments that some tubular and capsular dilatation can occur acutely from ureteral obstruction alone, so that this factor must be considered also in explaining the kidney changes in the case described in the present report.

SUMMARY

1. Two cases of complete anuria occurring during sulfapyridine therapy were observed.

2. In both cases anuria was due to calculi blocking the urinary tract at the ureterovesical orifices.

3. Treatment by means of cystoscopy was successful.

4. The pathologic changes in the upper urinary tract of a patient dying of a neurosurgical complication consisted essentially of great tubular and capsular dilatation, marked congestion and vacuolization within the glomerular tufts, and an acute hemorrhagic pyelo-ureteritis extending into the adjacent renal medullary tissue.

14. Blake, F. G., and Haviland, J. W.: Sulfapyridine in Pneumococcal, Streptococcal and Staphylococcal Infections, Tr. Am. Phys. **54:** 130, 1939.
15. Stryker, W. A.: The Nature of the Renal Lesion with Sulfapyridine Therapy, J. A. M. A. **114:** 953 (March 16) 1940.
16. Strong, K. C.: Plastic Studies in Abnormal Renal Architecture: V. The Parenchymal Alterations in Experimental Hydronephrosis, Arch. Path. **29:** 77 (Jan.) 1940.

PERIPHERAL NEUROPATHY DUE TO VITAMIN B_1 DEFICIENCY IN DIABETES MELLITUS

HARRY D. FEIN, M.D.
ELAINE P. RALLI, M.D.
AND
NORMAN JOLLIFFE, M.D.
NEW YORK

We are reporting nine cases of a symmetrical peripheral neuropathy due to vitamin B_1 deficiency found in a group of 422 ambulatory patients with diabetes mellitus. The occurrence of peripheral neuropathy in diabetic patients is well known and has been the subject of several reports since its description by Marchal de Calvi [1] in 1864. The incidence of this condition in groups of such patients varies, according to Jordan,[2] from 0.6 to 57.3 per cent. The extreme variation thus reported demands explanation and is due, in our opinion, to several factors. There is, first, a tendency on the part of many physicians to label vague pains in the extremities as neuritis without employing objective criteria for the diagnosis of peripheral neuropathy. Pain in the extremities of diabetic patients is common; it occurs in 17 per cent of Joslin's [3] patients. Such pain, however, is more often due to arterial and venous circulatory disturbances, arthritis, myositis or mechanical and fatigue phenomena than to peripheral neuropathy resulting from vitamin B_1 deficiency. Another factor is the failure to perform an adequate neurologic examination, especially in the absence of a history of pain in the extremities. Pain, though nearly always present at some time during the course of peripheral neuropathy, may be absent by the time the patient is examined, and its history can be elicited only by leading questions.

That vitamin deficiency may be an etiologic factor in the peripheral neuropathy of diabetic patients was first pointed out by Wohl [4] in 1926 on the basis of the dietary history, clinical observations and results of treatment with yeast and yeast concentrates of a patient with diabetes. Then in 1928 Angle [5] noted improvement in a case of "diabetic tabes" following a diet rich in vitamins. The following year Minot [6] encountered two diabetic patients with peripheral neuritis who improved slowly by taking large amounts of yeast concentrate. The work of Wechsler [7] and of Root and Rogers [8]

From the Department of Medicine, New York University College of Medicine, the Diabetic Clinic of the Third Medical Division, and the Medical Service of the Psychiatric Division, Bellevue Hospital.

1. Marchal de Calvi, C. J.: Recherches sur les accidents diabétiques et essai d'une théorie générale du diabète, Paris, P. Asselin, 1864.
2. Jordan, W. J.: Neuritic Manifestations in Diabetes Mellitus, Arch. Int. Med. **57:** 307 (Feb.) 1936.
3. Joslin, E. P.: The Treatment of Diabetes Mellitus, ed. 6, Philadelphia, Lea & Febiger, 1937.
4. Wohl, M. G.: Avitaminosis in the Course of Diabetes, J. A. M. A. **87:** 901 (Sept. 18) 1926.
5. Angle, F. E.: Tabes Diabetica: Report of a Case, U. S. Nav. M. Bull. **26:** 81 (Jan.) 1928.
6. Minot, G. R.: Some Fundamental Clinical Aspects of Deficiencies, Ann. Int. Med. **3:** 216 (Sept.) 1929.
7. Wechsler, I. S.: Unrecognized Cases of Deficiency Polyneuritis (Avitaminosis?): Preliminary Report, M. J. & Rec. **131:** 441 (May 7) 1930.
8. Root, H. F., and Rogers, M. H.: Diabetic Neuritis with Paralysis, New England J. Med. **202:** 1049 (May 29) 1930.

further suggested that these patients have, as a rule, an inadequate intake of food and vitamins and that their clinical and neuropathologic manifestations and response to treatment were similar to those of patients having beriberi.

Since then Vorhaus and his co-workers,[9] in 1935 and Sciclounoff and Broccard[10] in 1936, as a result of therapeutic application of thiamine hydrochloride, have stated that a deficiency of vitamin B_1 was the etiologic factor in the neuritis of diabetes. Unfortunately, neither of these groups described their criteria for the diagnosis of peripheral neuropathy or detailed the objective observations before and after treatment, although they mentioned in general pains, paresthesias, tenderness and altered reflexes.

On the other hand, Needles,[11] on the basis of careful dietary analysis, reported three cases of diabetes presenting definite peripheral neuropathy in which the diets were apparently adequate as judged by the vitamin B_1/calory ratio. A sample diet for a single day was utilized in these estimations. One of his patients freely admitted dietary infractions which would significantly lower this ratio. Substitution of food low in vitamin B_1 but containing equivalent carbohydrate and caloric values is frequent in all groups of diabetic patients and may explain how a prescribed adequate diet becomes actually inadequate in vitamin B_1.

The object of this study was to determine the incidence of definite peripheral neuropathy due to vitamin B_1 deficiency in a large group of diabetic patients and the response to specific therapy.

MATERIALS AND METHOD OF STUDY

The subjects in this study were all ambulant patients who attended the diabetic clinic of the Third (New York University) Division of Bellevue Hospital during 1939. Each patient was subjected to a neurologic examination specifically aimed at discovering evidence of peripheral neuropathy. A total of 422 patients were so examined. To avoid the diagnostic problem already discussed we have followed the criteria of one of us[12] for the diagnosis of peripheral neuropathy due to vitamin B_1 deficiency. These criteria require the presence of a definite bilateral symmetrical polyneuropathy involving first and predominantly the lower extremities. The minimum observations necessary to establish this diagnosis consist in sensory changes in a peripheral nerve distribution in the lower extremities (such as plantar hyperesthesia, which may extend up the ankles and legs in a sock distribution, tenderness of calf muscles and loss of position sense and of vibratory sensation, beginning first in the toes and later extending proximally) plus at least absence of ankle jerks. Peripheral neuropathy of this extent, limited to the lower extremities and with the knee jerks preserved, is designated as mild. If, in addition, the knee jerks are lost, the neuropathy is classified as moderate; if there is involvement of the upper extremities, the spinal cord or the cranial nerves, or if a "central neuritis" is present, it is classified as severe. Peripheral neuropathy that involves a single nerve, that is not bilateral and symmetrical, or does not involve first and predominantly the lower extremities (in ambulatory patients) is excluded as probably not due to vitamin B_1 deficiency alone. For such neuritides other etiologic agents should be sought. These, such as lead, arsenic, triorthocresol phosphate and bacterial and virus infections, may and do operate in the diabetic as well as in the nondiabetic person, and the type of peripheral neuropathy they produce seldom fulfils the criteria for the diagnosis of neuropathy due to B_1 deficiency.

All patients in whom the objective criteria necessary for the diagnosis of mild peripheral neuropathy were found were designated as suitable for a therapeutic test. Those having only suggestive signs were excluded. The designated patients, without otherwise changing their diet, were given 10 mg. of synthetic thiamine hydrochloride by mouth daily throughout the period of observation; follow-up observations were performed

TABLE 1.—*Clinical Data*

Case Number	Age	Sex	Duration Diabetes in Years	Diet: Carbohydrate	Diet: Protein	Diet: Fat	Insulin	Vitamin B_1 Calory Ratio	Status of Diabetic Control	Complications
1	53	♀	2	130	65	85	None	4.3	Diabetes out of control and untreated until seen in clinic; therapy started at same time	Arteriosclerotic and hypertensive heart disease
2	57	♀	5	150	65	75	20-0-15	4.1	Diabetes well controlled	Toxic adenoma of thyroid
3	63	♂	2	300	65	85	None	3.28	Poorly nourished; lived in municipal lodging house; only small amounts of sugar in urine; diet eaten not the one prescribed	Arteriosclerotic and hypertensive heart disease; chronic diffuse glomerulonephritis
4	56	♂	½	150	65	65	None	4.1	Diabetes uncontrolled; sugar in urine; diabetes controlled after start of therapy	Mild general arteriosclerosis
5	54	♀	6	250	65	87	None	3.5	Diabetes controlled	Arteriosclerotic and hypertensive heart disease
6	56	♀	12	300	65	80	None	3.28	Patient did not follow diet; always moderate glycosuria	Essential hypertension; postoperative thyroid
7	50	♂	2	200	65	65	40-20-40	3.2	Moderate glycosuria	Essential hypertension
8	72	♂	30	150	65	85	10-0-10	4.1	Moderate glycosuria	General arteriosclerosis; chronic cholecystitis
9	50	♀	4	140	80	60	None	4.1	Occasional mild glycosuria	Essential hypertension; mild hyperthyroidism

9. Vorhaus, M. G.; Williams, R. R., and Waterman, R. E.: Studies on Crystalline Vitamin B_1: Experimental and Clinical Observations, J. A. M. A. **105**: 1580 (Nov. 16) 1935.

10. Sciclounoff, François, and Broccard, Raymond: La vitamine B_1 dans le traitement des polynévrites, Schweiz. med. Wchnschr. **66**: 985 (Oct. 10) 1936.

11. Needles, William: Vitamin Studies in Cases of Diabetic Neuritis, Arch. Neurol. & Psychiat. **41**: 1222 (June) 1939.

12. Jolliffe, Norman: The Diagnosis, Treatment and Prevention of Vitamin B_1 Deficiency, Bull. New York Acad. Med. **15**: 469 (July) 1939.

weekly for a period of at least six months. All conditions remained constant except the adjustment of insulin as required.

RESULTS

Of a total of 422 patients, nine, or 2.1 per cent, fulfilled the criteria for the diagnosis of peripheral neuropathy resulting from vitamin B_1 deficiency. In these nine subjects there were no abnormal neurologic manifestations other than the peripheral neuropathy, and no other clinically evident vitamin deficiencies. In table 1 are presented the clinical data, such as age, sex, duration of diabetes, diet, use of insulin, status of diabetic control and complications. None of these patients had evidence of ketosis during the period of study. There were four men and five women, the ratio of males to females in the entire group of 422 subjects being approximately the same. All nine subjects were 50 years of age or over, while 69 per cent of the whole group of 422 patients were over 49 years of age. The known duration of the diabetes of the nine patients varied from six months to thirty years, with an average of 6.7 years. The average duration of diabetes in the 422 patients was 8.3 years.

The neurologic observations and the results of therapy are summarized in table 2. Tenderness of the calf muscles, plantar hyperesthesia and loss of ankle jerks were present in all nine subjects; some degree of loss of vibratory sensation was found in three, while the position sense was intact in all. No subject showed more than mild peripheral neuropathy according to our criteria. After therapy, plantar hyperesthesia disappeared in all cases after four weeks and in three after two weeks. Tenderness of the calves disappeared in all cases after six weeks and in five cases after two weeks. Vibratory sensation in the toes was absent in three subjects, returning to normal after eight and ten weeks respectively in two subjects but remaining absent in the toes of one subject (case 3) after six months of treatment. The ankle jerks returned after two weeks in one subject and within fourteen weeks in eight subjects; in one subject (case 3) they had not returned at the end of six months.

Some patients not tabulated in this study complained of persistent unilateral pain in an extremity, while others experienced vague aches and pain in the extremities. Neurologic examination of these patients disclosed no objective signs of bilateral symmetrical peripheral neuropathy. These subjects were treated with thiamine hydrochloride, vegex or brewers' yeast. The results were not uniform. In some the relief was apparently sustained; in others it was temporary, while in still others no relief was experienced.

COMMENT

We believe that the symmetrical peripheral neuropathy found in these nine diabetic patients was due to vitamin B_1 deficiency. This belief is based on the following reasons: First, the clinical characteristics fulfilled the established criteria for the diagnosis of peripheral neuropathy due to vitamin B_1 deficiency; second, without otherwise changing the diet or therapy, the addition of 10 mg. of synthetic thiamine hydrochloride daily by mouth was followed by cure in eight cases and by objective improvement in the ninth.

The explanation of the development of peripheral neuropathy due to vitamin B_1 deficiency in these nine subjects is speculative, but in our opinion it is due directly to eating a diet of borderline adequacy in vitamin B_1. On the basis of Cowgill's [13] prediction formula, the diets prescribed for these patients were all adequate in that the vitamin B_1/calory ratio ranged from 3.2 to 4.3, representing an excess of 140 to 210 per cent over their predicted minimal requirements. One of us [14] has recently suggested that diets representing a vitamin B_1/calory ratio of 2.3 or more are definitely adequate, those less than 1.7 are definitely inadequate, and those between 1.7 and 2.3 are of borderline adequacy. By this criterion all the prescribed diets were above the borderline range, furnishing safety margins of from 39 to 87 per cent. As we had previously pointed out, however, substitution of foods poor in vitamin B_1 (such as white bread or crackers) but containing equivalent carbohydrate and caloric values for prescribed foods richer in vitamin B_1 is common in all groups of diabetic patients. This was especially true in our patients because of their poor economic condition. In view of this it is surprising that a peripheral symmetrical polyneuropathy developed in but 2.1 per cent of the patients. There are, moreover, several other possible contributory factors. The most important of these, we believe, may be arteriosclerosis. This is suggested by the age distribution of our patients. Woltman and Wilder,[15] in a study of the peripheral nerves of ten diabetic patients, observed arteriosclerosis of the small arteries in the nerve tunnels of the legs of all subjects and areas of degeneration in the nerves of nine subjects. This vascular inadequacy may require a

TABLE 2.—*Number of Weeks After Beginning of Treatment When Reversal of Symptoms Were Noted* *

		Sensory			Motor	
Case	Weeks of Treatment	Calf Tenderness	Plantar Hyperesthesia	Vibratory Sensation in Toes	Ankle Jerks	Knee Jerks
1	0	+	+	N	0	+
	3	0	0	N	0	+
	8	0	0	N	+	+
2	0	+	+	N	0	+
	3	0	+	N	0	+
	4	0	0	N	0	+
	9	0	0	N	+	+
3	0	+	+	0	0	+
	2	0	+	0	0	+
	3	0	0	0	0	+
	24	0	0	0	0	+
4	0	+	+	0	0	+
	4	+	0	0	0	+
	6	0	0	0	0	+
	10	0	0	+	0	+
	12	0	0	+	+	+
5	0	+	+	N	0	+
	3	0	0	N	+	+
	4	0	0	N	+	+
6	0	+	+	N	0	+
	2	0	0	N	0	+
	4	0	0	N	+	+
7	0	+	+	N	0	+
	2	0	+	N	0	+
	3	0	0	N	0	+
	12	0	0	0	+	+
8	0	+	+	0	0	+
	2	0	0	0	0	+
	8	0	0	+	0	+
	14	0	0	+	+	+
9	0	+	+	N	0	+
	2	0	0	N	+	+

* 0 indicates absence; + presence, and N normal.

13. Cowgill, G. R.: The Vitamin B Requirement of Man, New Haven, Conn., Yale University Press, 1934.

14. Jolliffe, Norman: A Clinical Evaluation of the Adequacy of Vitamin B_1 in the American Diet, Internat. Clin. 4: 46 (Dec.) 1938.

15. Woltman, H. W., and Wilder, R. M.: Diabetes Mellitus: Pathologic Changes in the Spinal Cord and Peripheral Nerves, Arch. Int. Med. 44: 576 (Oct.) 1929.

higher concentration of thiamine in the blood, to provide sufficient vitamin to the nerves, than in subjects with normal arteries, as pointed out by Naide.[16] Another factor may be the polyuria[13] accompanying glycosuria, which, if persistent, may cause an increased excretion of vitamin B_1 in the urine, rendering it less available for use by the body. This factor may have played a role in six of our nine subjects who, because of lack of cooperation, either voluntary or due to economic circumstances, showed persistent though moderate glycosuria without ketosis. Another factor, of doubtful importance, may be the presence of a disturbance in carbohydrate metabolism in diabetic persons which might conceivably interfere with the utilization of thiamine hydrochloride. Too little is known concerning this relationship to deny its influence, but two facts are available that cast doubt on its significance. The first is that peripheral neuropathy in our subjects occurred in the older age group with relatively mild diabetes, rather than in the younger group with the more severe diabetes. The second fact is that thiamine hydrochloride administered by mouth caused prompt improvement, showing that these diabetic patients could utilize from this amount of the vitamin given by mouth enough to cure or improve the clinical manifestations of the deficiency. Another factor, which does not seem to apply to any of our patients but which under certain conditions may be contributory, is the institution of insulin therapy and the resulting increased utilization of carbohydrate. In subjects whose stores and intakes of vitamin B_1 are of borderline adequacy, the increased utilization of carbohydrate will require additional vitamin B_1. Unless precautions are instituted, polyneuropathy may result from vitamin B_1 deficiency. Hausman[17] has recently observed three such cases. In this connection it is interesting to note that Sydenstricker, Geeslin and Weaver[18] observed the development of clinical signs of pellagra in two diabetic patients when the carbohydrate content of the diet was increased and added insulin was administered to insure utilization of the augmented diet. They concluded that, "under chronic conditions, signs of avitaminosis might be expected to appear, with or without ketosis, when unusually rapid dextrose metabolism is brought about by the use of insulin."

SUMMARY

We have studied 422 ambulant diabetic patients. Nine (2.1 per cent) had a symmetrical peripheral neuropathy characteristic of the peripheral neuropathy found in subjects having proved vitamin B_1 deficiency. Treatment by daily administration of 10 mg. of thiamine hydrochloride by mouth, without otherwise changing the regimen, resulted in cure of eight subjects and improvements in the ninth.

Indifferent or inconsistent results were obtained on treating neuropathy of single nerves or the vague aches and pains of the diabetic patient.

CONCLUSIONS

The symmetrical peripheral neuropathy beginning first in, and involving primarily, the lower extremities of patients having diabetes mellitus responds to thiamine hydrochloride and in our opinion is due to vitamin B_1 deficiency.

16. Naide, Meyer: The Use of Vitamin B_1 in Rest Pain of Ischemic Origin, Am. J. M. Sc. **197**: 766 (June) 1939.
17. Hausman, Louis: Personal communication to the authors.
18. Sydenstricker, V. P.; Geeslin, L. E., and Weaver, J. W.: Avitaminosis Occurring in Diabetic Patients Under Insulin Therapy, J. A. M. A. **113**: 2137 (Dec. 9) 1939.

THE COEXISTENCE OF BRUCELLA INFECTION AND HODGKIN'S DISEASE

A CLINICAL, BACTERIOLOGIC AND IMMUNOLOGIC STUDY

N. BOWMAN WISE, M.D.
AND
MARY A. POSTON, M.A.
DURHAM, N. C.

The isolation of Brucella melitensis from cultures of lymph nodes from patients having Hodgkin's disease opened an interesting field of investigation.[1] Subsequently fourteen consecutive cases of Hodgkin's disease have been studied carefully for evidence of Brucella infection. The clinical, bacteriologic and immunologic observations in seven cases in this series are presented in detail and in the remainder are summarized briefly.

Cultures have been taken of a part of every excised lymph node[2] and the remaining part has been prepared for pathologic study. In every case the clinical diagnosis of Hodgkin's disease has been confirmed by histologic section of the lymph nodes, taken for biopsy, and the existence of Brucella infection has been demonstrated by the isolation of the organisms from either the blood or the lymph nodes or both. The agglutinin-absorption tests and the bacteriostatic reactions of dyes have been used to determine the species of Brucella. The technics used for the agglutination reaction and for the determination of the opsonocytophagic index have been previously reported.[3] Because the Brucella organisms isolated from patients with Hodgkin's disease have been found to differ significantly from the usual laboratory strains,[4] agglutination reactions and opsonocytophagic index determinations have recently been carried out both with the usual laboratory Brucella strain and with an encapsulated strain isolated from a patient having Hodgkin's disease. The opsonocytophagic index number has been calculated by the method of Foshay and Le Blanc.[5]

The cases are reported here in the sequence in which they came under observation.

REPORT OF CASES

CASE 1.—R. P., a white man aged 24, who entered the hospital on Oct. 26, 1938, had become ill in November 1937 with enlargement of the right cervical lymph nodes and he was treated by excision and superficial radium therapy. At the time of entry a lymph node from 3 to 4 cm. in diameter and several smaller nodes were palpable in the right cervical region. Brucella melitensis var. suis was isolated from a right cervical lymph node which had the characteristic histopathologic appearance of Hodgkin's disease. The enlarged lymph nodes regressed under treatment with sulfanilamide and serum from a person considered immune to Brucella infection. The patient was discharged from the hospital Dec. 27, 1937, and was followed at close intervals. There was no evidence of activity

Dr. Wise is James A. Greene Research Fellow for the Study of Brucellosis.

From the Department of Medicine and the Department of Bacteriology, Duke University School of Medicine.

1. Parsons, P. B., and Poston, Mary A.: The Pathology of Human Brucellosis, South. M. J. **32**: 7-13 (Jan.) 1939. Poston and Parsons.[2]
2. Poston, Mary A., and Parsons, P. B.: Isolation of Brucella from Lymph Nodes, J. Infect. Dis. **66**: 86-90 (Jan.-Feb.) 1940.
3. Menefee, E. E., Jr., and Poston, Mary A.: Significance of Standard Laboratory Procedures in the Diagnosis of Brucellosis, Am. J. M. Sc. **197**: 646-653 (May) 1939.
4. Mickle, W. A.: Capsule Formation by Members of the Brucella Group, J. Infect. Dis. **66**: 271 (May-June) 1940.
5. Foshay, Lee, and Le Blanc, T. J.: The Derivation of an Index Number for Opsonocytophagic Test, J. Lab. & Clin. Med. **22**: 1297-1301 (Sept.) 1937.

of the Hodgkin's disease process until January 1940, when the right cervical lymph nodes again enlarged. Repeated cultures taken of the blood and lymph nodes have been negative.

It is considered that further observation is necessary to determine the true significance of the isolation of Brucella from this patient.

CASE 2.—*Enlargement of cervical, axillary, inguinal and mediastinal lymph nodes of ten months' duration; culture of a cervical node yielded Brucella melitensis var. melitensis; regression of enlargement of lymph nodes under sulfapyridine therapy; recurrent enlargement of inguinal and femoral lymph nodes on the left; Brucella melitensis var. melitensis isolated from blood cultures; treatment with sulfapyridine and immune serum; temporary improvement.*

M. W., a Negro boy aged 5 years, who was brought to the hospital Nov. 16, 1938, had enlargement of the neck of ten months' duration. In February 1938 a firm, painless swelling appeared below the angle of the left jaw which alternately subsided and recurred. For a week preceding the hospital visit the patient had had a mild cold with nonproductive cough, and a tender swelling had appeared in the left groin.

On physical examination the temperature was 37 C. (98.6 F.), the pulse rate 120 and the respiratory rate 20. The child was well nourished and did not appear ill. There was a firm, nontender mass of lymph nodes measuring 6 by 8 cm. in the left cervical region. The right cervical nodes were enlarged to a lesser degree. The left axillary nodes were markedly enlarged, one node measuring 4 cm. in diameter. The right axillary and inguinal nodes were enlarged. Retromanubrial dulness measured 5 cm. The heart and lungs were not remarkable. There was no abdominal tenderness and no organs were palpable. On rectal examination a firm, nontender mass was felt on the left side.

Wassermann and Kahn reactions of the blood were negative; examination of the blood showed hemoglobin 62 per cent, white blood cells 16,700, with polymorphonuclear leukocytes 80 per cent (stab cells 12 per cent), eosinophils 0, basophils 0, large lymphocytes 3 per cent, small lymphocytes 17 per cent and monocytes 0; Brucella agglutination was negative; an intracutaneous tuberculin test (1 : 1,000) gave negative results.

Permission for the biopsy of a lymph node was refused and the patient was not seen again until December 7. His condition had remained unchanged until the preceding five days, when loss of appetite and an evening elevation of temperature developed. Physical examination was unchanged except for a slight increase in the size of the enlarged lymph nodes. Biopsy of a cervical node confirmed the clinical diagnosis of Hodgkin's disease and a culture taken of this node yielded Brucella melitensis var. melitensis. Admission to the hospital was advised but the patient did not return until Jan. 26, 1939.

The physical condition at this admission was unchanged except for further slight enlargement of the lymph nodes. The temperature was 39.5 C. (103.1 F.), pulse rate 140 and respiratory rate 24. A blood count revealed hemoglobin 62 per cent, red blood cells 3,140,000 and white blood cells 20,000, polymorphonuclear leukocytes 82 per cent (stab cells 53 per cent), eosinophils 1 per cent, basophils 0, large lymphocytes 4 per cent, small lymphocytes 9 per cent, monocytes 4 per cent. Roentgenograms of the chest showed a large mass in the superior mediastinum. Bacteriologic and immunologic studies are given in chart 1.

At bed rest the patient's temperature fell to 37.5 C. (99.3 F.) on the third hospital day, at which time administration of sulfapyridine was started but it was discontinued after one week because of leukopenia. Throughout the administration of sulfapyridine the patient was afebrile, but four days after discontinuation of the drug his temperature rose to 39.5 C. (103.1 F.) and remained elevated for two days. Blood cultures were sterile. Under sulfapyridine therapy there was a progressive and marked decrease in the size of the superficial lymph nodes, and x-ray examination showed marked diminution in the size of the mediastinal mass. A lymph node excised on February 11 again showed the histopathologic picture of Hodgkin's disease. A culture taken of this node yielded diphtheroids. The patient had improved greatly by the time of discharge on March 3 and appeared well when visited at home on March 18.

The patient was readmitted to the hospital on May 17, having felt well in the interval. The temperature was 36.8 C. (98.6 F.). There was no recurrent enlargement of the cervical, axillary and right inguinal lymph nodes but there was definite enlargement of the left inguinal and femoral nodes. Hemoglobin was 59 per cent; red blood cells numbered 3,020,000, white blood cells 8,800, polymorphonuclears 52 per cent, eosinophils 2 per cent, basophils 0, large lymphocytes 6 per cent, small lymphocytes 34 per cent and monocytes 6 per cent. Cultures taken of an inguinal node on the left side which gave the pathologic appearance of Hodgkin's disease were sterile. A roentgenogram of the chest showed complete absence of the mass originally noted in the superior mediastinum.

On May 19 sulfapyridine was given but was discontinued on May 27 because of severe nausea and vomiting. On May 22 the patient's temperature, previously not above 37.8 C. (100 F.), rose to 39 C. (102 F.) and remained elevated for four days. At this time Brucella melitensis var. melitensis was isolated from the blood. Ten cc. of bovine antimelitensis serum was given intramuscularly on May 24 and 25, with a subsequent prompt fall of temperature to normal. The left inguinal and

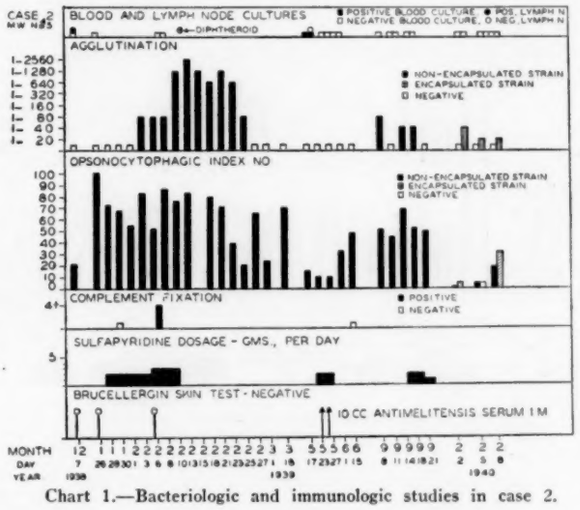


Chart 1.—Bacteriologic and immunologic studies in case 2.

femoral lymph nodes gradually decreased in size. On May 29 the patient complained of generalized itching of the skin and a mild exfoliative dermatitis developed. He was discharged from the hospital greatly improved on June 4.

The patient was readmitted to the hospital on September 8. He had been well until one week previously, when an evening fever developed and recurrent enlargement of the left cervical, axillary and inguinal lymph nodes. The temperature was 37.4 C. (99.3 F.). The patient did not appear ill. The firm, nontender cervical nodes were barely palpable. In the left axilla was a mass of firm, nontender nodes measuring 5 by 6 cm. The inguinal nodes were similarly enlarged. A large, firm, nontender mass measuring 6 by 6 cm. was felt over the right external iliac vessels. On rectal examination a similar smaller mass was felt on the left side.

Examination of the blood revealed hemoglobin 58 per cent, red blood cells 2,750,000, white blood cells 5,200, polymorphonuclears 44 per cent (stab cells 3 per cent), eosinophils 2 per cent, basophils 0, large lymphocytes 3 per cent, small lymphocytes 36 per cent, monocytes 15 per cent. The corrected sedimentation rate was 28 mm. per hour. A roentgenogram of the chest showed no mediastinal or hilar enlargement.

An elevation of temperature to 38.6 C. (101.5 F.) was noted on the second hospital day. Thereafter the patient was afebrile for one week, when the temperature rose to 38.2 C. (100.7 F.). At this time sulfapyridine was given for one week, during which time the fever promptly ceased and there was marked

regression of lymph node enlargement by the time of discharge on September 23.

The patient returned to the hospital on Feb. 2, 1940. In the interval he had had occasional episodes of fever and malaise lasting several days. One week before his return there was transient enlargement of the left cervical lymph nodes.

The temperature was 37.4 C. (99.3 F.). The left cervical lymph nodes were firm and nontender and measured from 2 to 3 cm. in diameter. The right cervical, axillary and inguinal nodes were smaller, firm and nontender. On rectal examination a few small, firm nodes were palpable on the left.

Examination of the blood revealed hemoglobin 68 per cent, red blood cells 3,760,000, white blood cells 12,600, polymorphonuclears 69 per cent (stab cells 1 per cent), eosinophils 1 per cent, basophils 0, large lymphocytes 2 per cent, small lymphocytes 27 per cent, monocytes 1 per cent; corrected sedimentation rate 28 mm. per hour. A roentgenogram of the chest was not remarkable.

During the patient's hospital stay there was an occasional elevation of temperature to 37.7 C. (99.8 F.). No treatment was given and the patient's condition was unchanged at discharge on February 11.

The initial marked regression of the widespread enlargement of lymph nodes under sulfapyridine therapy in this case was striking. It is noteworthy that the

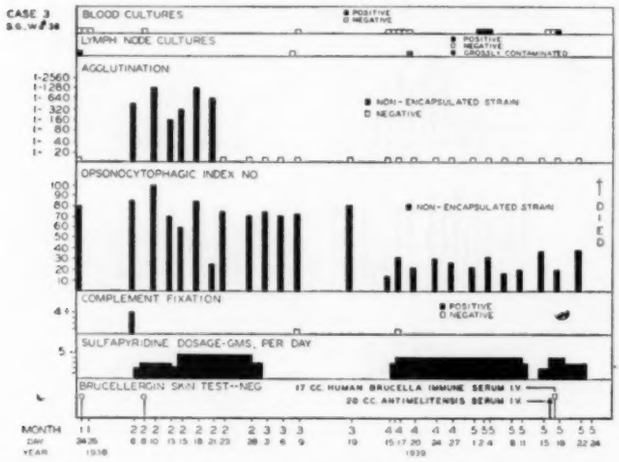


Chart 2.—Bacteriologic and immunologic studies in case 3.

appearance of serum agglutinins and marked phagocytosis coincided with this clinical improvement. Subsequently Brucella melitensis var. melitensis was isolated from blood cultures, taken during a febrile episode and shortly after recurrent enlargement of the left inguinal and femoral lymph nodes. After administration of antimelitensis serum and sulfapyridine there was prompt subsidence of fever and lymph node enlargement. No evidence of an immune response existed at the time Brucella melitensis var. melitensis was isolated from the blood, nor has there been any significant immune response during subsequent periods of activity of the disease process. The clinical course, which has appeared to be influenced by treatment directed toward control of the Brucella infection, can be correlated closely enough with the cultural and immunologic observations to suggest that a great part of the clinical picture presented by this patient with Hodgkin's disease might be explained by the coexisting Brucella infection.

CASE 3.—*Left supraclavicular lymph node enlargement; roentgen therapy; fever and enlargement of liver and spleen, isolation of Brucella melitensis var. melitensis from lymph node and blood cultures; treatment with sulfapyridine; death one year after onset.*

S. G., a white man aged 38, admitted to the hospital Jan. 20, 1939, complained of abdominal pain of five weeks' duration. His illness began in April 1938 with a gradual onset of weakness, painless progressive enlargement of the left supraclavicular lymph nodes and intermittent sharp pain in the lower part of the abdomen radiating to both lumbar regions. A loss of weight of from 20 to 30 pounds (9 to 13.6 Kg.) occurred during the first month of illness. Roentgen therapy was given to the left supraclavicular region during April and May 1939, with prompt regression of lymph node enlargement and improvement in the patient's general condition. The patient was relatively well and able to work until December 1938, when so-called flu developed, with malaise, fever and night sweats. At this time severe "knifelike" para-umbilical pain, radiating to both lumbar regions, appeared and persisted.

The temperature was 38.5 C. (101.3 F.), pulse rate 104, respiratory rate 22 and blood pressure 110 systolic, 72 diastolic. The patient was malnourished and appeared chronically ill. Small, firm, nontender cervical and axillary nodes were palpable on the left side. There was no other enlargement of the lymph nodes. The abdomen was distended and tympanitic but not tender. The liver edge was percussed 3 cm. below the costal margin. The spleen was palpable at the costal margin.

Wassermann and Kahn reactions of the blood were negative; hemoglobin was 61 per cent; red blood cells numbered 3,570,000, white blood cells 5,900, polymorphonuclears 85 per cent (stab cells 2 per cent), eosinophils 1 per cent, basophils 0, large lymphocytes 4 per cent, small lymphocytes 3 per cent and monocytes 7 per cent. The corrected sedimentation rate was 24 mm. per hour; roentgenographic examinations of the chest and gastrointestinal tract were negative except for an inconstant defect of the duodenal cap thought to be due to extrinsic pressure. Histologic section of an axillary lymph node showed lymphadenitis suggestive of Hodgkin's disease and cultures taken of this node yielded Brucella melitensis var. melitensis. Bacteriologic and immunologic studies are given in chart 2.

At rest in bed the patient's temperature varied between 38 and 39 C. (100.4 and 102 F.). Administration of sulfapyridine was started on February 7 but was discontinued on March 1 because of leukopenia and anemia. During sulfapyridine therapy the patient became afebrile, the abdominal pain disappeared and the liver and spleen decreased in size. Cultures taken of a lymph node excised on March 8 were sterile. This node again showed a histopathologic picture suggestive of Hodgkin's disease. The patient was much improved at the time of discharge, March 11, although for the three preceding days an elevation of temperature to 38.4 C. (101.1 F.) was noted.

The patient remained well for one week and then an infection of the upper respiratory tract developed, following which he became acutely ill and was readmitted to the hospital April 15.

The temperature was 38.9 C. (102 F.), pulse rate 124, respiratory rate 24, and blood pressure 110 systolic, 80 diastolic. The patient was markedly emaciated and acutely ill. The essential physical conditions were unchanged.

Hemoglobin was 60 per cent, red blood cells numbered 3,000,000, white blood cells 12,320, polymorphonuclears 92 per cent (stab cells 7 per cent, juveniles 1 per cent), eosinophils 0, basophils 0, large lymphocytes 3 per cent, small lymphocytes 3 per cent, monocytes 2 per cent. The corrected sedimentation rate was 26 mm. per hour. A roentgenogram of the chest showed no significant change. An examination of the gastrointestinal tract again showed inconstant deformity of the duodenal bulb. Brucella melitensis var. melitensis was isolated from blood cultures. Sections of an axillary node showed the microscopic appearance of Hodgkin's disease. Cultures taken of this node were grossly contaminated.

The patient's course was characterized by fever and progressive cachexia, terminating in death six weeks after admission. Sulfapyridine was started on the second hospital day and was continued until the day before death. Repeated blood transfusions were given. On May 14, intravenous administration of bovine antimelitensis serum had to be stopped after 20 cc. had been given because of severe pain in the back. Seventeen cc. of blood serum from a person who had recovered from Brucella infection was given intravenously on May 20. Signs of focal pneumonia appeared and the patient sank into coma and died May 24.

Necropsy showed Hodgkin's disease involving the spleen, liver, kidneys and all lymph nodes, especially the retroperitoneal

and abdominal nodes. Cultures taken of the liver, a splenic lesion, lungs, pancreas, testicle, bile and of many lymph nodes yielded Brucella melitensis var. melitensis.

When this patient first came under observation, Hodgkin's disease with extensive abdominal involvement was considered to be the probable diagnosis. It should be emphasized, however, that the diagnosis of Hodgkin's disease was not established until six weeks before death. The histopathologic appearance of the first lymph nodes of which a biopsy was made was suggestive, but conclusive evidence of Hodgkin's disease was not obtained until a third biopsy was made. On the contrary, the presence of Brucella infection was demonstrated by isolation of the organism from the first lymph node biopsy five months before death and from subsequent blood cultures. Coincident with this clinical improvement was the appearance of serum agglutinins and marked phagocytosis. However, evidence of immunity to Brucella subsequently disappeared during the rapidly progressive phase of the disease, which was characterized by fever, cachexia and bacteremia. At necropsy Hodgkin's disease was widespread, and cultures taken of numerous lymph nodes and of the liver, spleen, pancreas, testicle and bile yielded Brucella melitensis var. melitensis.

CASE 4.—W. D., a white man aged 31, who entered the hospital Feb. 14, 1939, complained of intermittent fever, malaise and loss of weight of two years' duration. Coincident with the onset of these symptoms a tender swelling was noted in the right cervical region which regressed after roentgen therapy, but the systemic symptoms continued. Several weeks before entry enlargement of the right cervical lymph nodes was noted. Several firm, nontender right cervical nodes, about 2 cm. in diameter, were felt, and there was slight enlargement of the left cervical and axillary nodes. The spleen was palpable at the costal margin. Biopsy of a cervical lymph node established the diagnosis of Hodgkin's disease. Cultures of the nodes were sterile. Under treatment with sulfapyridine there was a definite decrease in the size of the enlarged lymph nodes. This treatment had to be discontinued because of the development of icterus, which persisted. The patient's subsequent course was characterized by Pel-Ebstein fever and progressive cachexia. Death occurred November 22. Permission for necropsy was not obtained. Brucella melitensis var. suis was isolated from the blood during the last four months of life.

CASE 5.—*Generalized pruritus of nine months' duration; right cervical and mediastinal lymph node enlargement; isolation of Brucella melitensis var. suis from blood and lymph node cultures; treatment with sulfapyridine; no improvement.*

P. T., a white woman aged 31, who entered the hospital on Feb. 18, 1939, complained of generalized pruritus of nine months' duration. No cutaneous lesions other than scratch marks had been noted. Three weeks before admission she noticed prominence of a vein in the left side of her neck. A loss of 10 pounds (4.5 Kg.) had occurred.

On physical examination the temperature was 36.9 C. (98.4 F.), pulse rate 110, blood pressure 124 systolic, 82 diastolic. The patient was malnourished but did not appear ill. The skin was rough and dry; no lesions were noted. In the right cervical region a firm, nontender mass of lymph nodes, each about 1 cm. in diameter, was felt. Elsewhere there was no enlargement of the lymph nodes. The left external jugular vein was greatly distended. The chest and abdomen were not remarkable.

Wassermann and Kahn reactions of the blood were negative; hemoglobin was 77 per cent; red blood cells numbered 3,880,000 and the white blood cells 10,150, polymorphonuclears 67 per cent, eosinophils 8 per cent, basophils 0, large lymphocytes 5 per cent, small lymphocytes 8 per cent, monocytes 12 per cent; a roentgenogram of the chest showed a large mass in the superior mediastinum. A specimen taken from a right cervical lymph node for biopsy confirmed the diagnosis of Hodgkin's disease. Brucella melitensis var. suis was isolated from this node and from the blood. Immunologic studies are given in chart 3.

The patient was afebrile throughout her hospital stay. Sulfapyridine was given daily in doses up to 4 Gm. She was discharged March 10 but was closely followed and continued to take sulfapyridine. By March 27 there had been a definite reduction in the size of the right cervical nodes and pruritus had lessened. X-ray examination showed no change in the size of the mediastinal mass. Sulfapyridine was discontinued on April 3.

The patient returned on April 19 complaining of intensified pruritus of four days' duration. Physical examination was unchanged except for enlargement of a single, firm, nontender lymph node just above the right clavicle. A roentgenogram showed no change in the size of the mediastinal mass. Admission to the hospital for further treatment was advised but the patient refused. Sulfapyridine was taken irregularly from April 22 to April 30. The patient's condition was unchanged when last seen, May 1, 1939.

In this case there was definite reduction in the size of the enlarged right cervical lymph nodes under sulfapyridine therapy and pruritus improved, although no actual decrease in the size of the mediastinal mass could

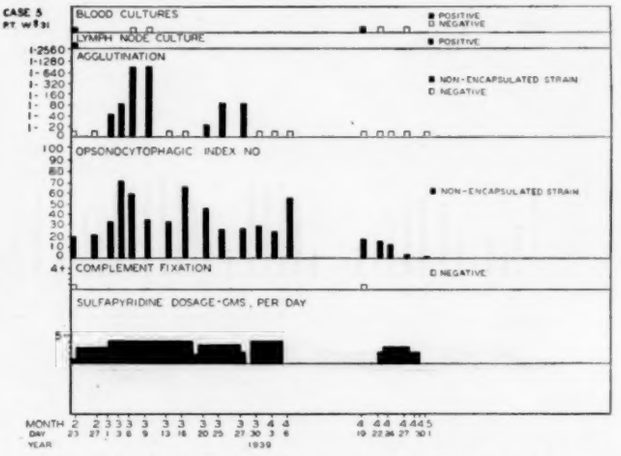


Chart 3.—Bacteriologic and immunologic studies in case 5.

be demonstrated roentgenologically. Serum agglutinins and significant degrees of phagocytosis appeared during the course of therapy but were not well sustained and were completely lacking with the recurrence of superficial lymph node enlargement, intensified pruritus and bacteremia. At this time Brucella melitensis var. suis was isolated from the heart's blood of two guinea pigs, which died nine days after intraperitoneal injection of 2 cc. of the patient's citrated blood.[6]

CASE 6.—C. I., a white woman aged 49, complained that in June 1938 fatigability and intermittent fever developed, with gradual painless enlargement of the superficial lymph nodes. Examination in January 1939 revealed marked enlargement of cervical, axillary, mediastinal and inguinal lymph nodes, and the liver and spleen were palpable. Biopsy of a lymph node established the diagnosis of Hodgkin's disease. Under roentgen therapy enlargement of the lymph nodes disappeared, the spleen and liver were no longer palpable and the fever subsided. She entered the hospital two weeks after completion of the roentgen therapy. Several firm, nontender cervical nodes on the right, from 2 to 3 cm. in diameter, were palpable. An excised lymph node showed marked fibrosis attributed to roentgen therapy and a culture taken of this node yielded Streptococcus viridans. The patient was closely followed and on May 1 slight enlargement of a right cervical node and an elevation of temperature

6. Poston, Mary A.: Studies on Chronic Brucellosis: III. Methods Used in Obtaining Cultures, Pub. Health Rep. **53**: 1-4 (Jan. 7) 1938.

were noted. Brucella melitensis var. melitensis was isolated from a blood culture taken on May 27, 1939. The patient was readmitted to the hospital June 6. There were daily elevations of temperature to 37.9 C. (100.2 F.), the spleen was palpable but there was no further enlargement of the lymph nodes. Under treatment with sulfapyridine and bovine antimelitensis serum the fever subsided, the cervical lymph nodes decreased in size and the spleen was no longer palpable at the time of discharge, June 15. Repeated blood cultures were sterile. Since this time there has been no evidence of activity of the Hodgkin's disease process.

CASE 7.—*Generalized pruritus with intermittent left cervical and axillary lymph node enlargement of three years' duration; initial treatment with sulfapyridine; recurrence of lymph node enlargement with stomatitis; cultures taken of oral lesions and of blood yielded Brucella melitensis var. melitensis; treatment with sulfapyridine and immunotransfusion; subsequent recurrence of cervical and axillary lymph node enlargement, appearance of mediastinal enlargement and fever; temporary improvement under roentgen therapy.*

M. T., a white woman aged 31, first visited the hospital Nov. 4, 1937, complaining of generalized itching of one year's duration. Her illness began in the autumn of 1936 with persistent generalized itching and no cutaneous lesions other than excoriations caused by scratching. There had been progressive abdominal enlargement and amenorrhea for the past five months, the patient considering herself pregnant.

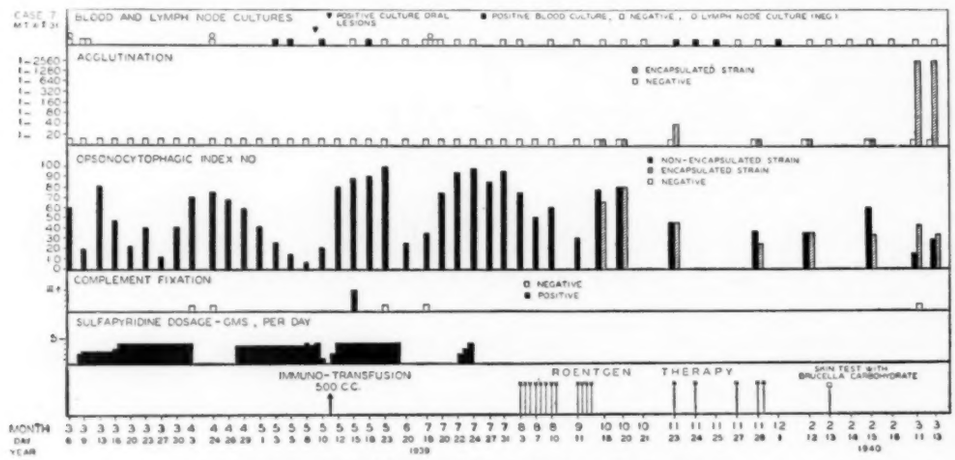


Chart 4.—Bacteriologic and immunologic studies in case 7.

The temperature was 37.7 C. (99.8 F.), the pulse rate 80, respiratory rate 20 and blood pressure 110 systolic, 65 diastolic. The patient was well nourished and did not appear ill. Small excoriations were scattered over the dry and scaly skin. No lymph nodes were palpable. Heart and lungs were not remarkable. The abdomen was symmetrically enlarged; the uterine fundus extended 22 cm. above the umbilicus. The clinical impression was neurogenic pruritus accentuated by pregnancy.

The patient returned on March 6, 1939, thirteen months after delivery of a normal fetus at term; she still complained of itching, which had continued with only brief periods of abatement. Enlargement of several left cervical and axillary lymph nodes had been noted for two months. On close questioning it was found that at the onset of her illness in November 1936 the patient had noted a firm, nontender mass the size of "the end of a thumb" in the left side of her neck, and soon afterward similar masses had been felt in the same region and in the left axilla. These masses had fluctuated in size but had been enlarging for the preceding two months. The patient had not given this history at the time of her first visit in November 1937 because she considered it of no significance. During the preceding year she had noticed thickening, dryness and slight darkening of her skin, a loss of 20 pounds (9 Kg.), and increasing fatigability and nervousness. There had been no return of the menses following parturition.

She was admitted to the hospital March 8, 1939. The temperature was 37 C. (98.6 F.), pulse rate 110, respiratory rate 22 and blood pressure 142 systolic, 80 diastolic. The patient was malnourished but did not appear ill. She constantly scratched all parts of her body, over which the skin was thickened, dry, a light brown and covered with numerous excoriations. The firm, nontender cervical lymph nodes, particularly those on the left, were enlarged to from 2 to 3 cm. in diameter. The left axillary nodes were enlarged to a slightly less degree. Elsewhere the superficial lymph nodes were barely palpable. The heart and lungs were not remarkable. There was no abdominal tenderness and no organs or masses were felt.

The Wassermann and Kahn reactions were negative; a blood count revealed hemoglobin 78 per cent, red blood cells 4,200,000, white blood cells 14,040, polymorphonuclears 76 per cent, eosinophils 11 per cent, basophils 1 per cent, large lymphocytes 4 per cent, small lymphocytes 6 per cent, monocytes 2 per cent. A roentgenogram of the chest was negative. Biopsy of a cervical lymph node confirmed the diagnosis of Hodgkin's disease. Cultures of the node were sterile. Bacteriologic and immunologic studies are given in chart 4.

Sulfapyridine was started on March 9 and was continued throughout her hospital stay. An occasional elevation of temperature to 38.5 C. (101.3 F.) was noted. The enlarged lymph nodes had decreased markedly in size and pruritus was much improved by the time of discharge, April 4.

For two weeks preceding her return on April 24 the patient noted a gradual recurrence of all her symptoms. The temperature was 37.2 C. (98.9 F.), pulse rate 90 and respiratory rate 20. The only change in her physical manifestations related to the size of the lymph nodes. The firm, discrete and nontender left cervical and axillary nodes were again enlarged, being from 2 to 3 cm. in diameter. The right cervical and axillary nodes were enlarged to a lesser degree. Hemoglobin was 81 per cent, red blood cells numbered 4,080,000 and white blood cells 14,400, polymorphonuclears 74 per cent (stab cells 9 per cent), eosinophils 2 per cent, basophils 0, large lymphocytes 2 per cent, small lymphocytes 17 per cent and monocytes 5 per cent. A roentgenogram showed two small areas of density in the right midlung field. Biopsy of a cervical lymph node revealed the histopathologic picture of Hodgkin's disease. Cultures of this node were sterile.

The patient was followed at short intervals until readmission to the hospital was possible. Administration of sulfapyridine, started on April 26, was attended by nausea and occasional vomiting. No change occurred in the size of the enlarged lymph nodes up to the time of readmission on May 7. Fever was absent during this period. A repeated roentgenogram of the chest on May 8 showed a slight decrease in the size of the densities in the right midlung field. On May 9 an elevation of temperature to 38 C. (100.4 F.) occurred and the patient complained of soreness of the mouth. Over the gums, buccal surfaces and hard palate were numerous irregularly outlined, white, adherent patches of exudate surrounded by hyperemic mucosa and measuring from 1 mm. to 1 cm. in diameter. The anterior pillars were reddened, but no lesions were noted in the pharynx. Cultures taken of material from the oral lesions yielded Streptococcus viridans, Neisseria siccus and Brucella melitensis var. melitensis. There was no growth on Sabouraud's medium and no spirochetes were seen on dark field examination of material from the lesions. Brucella melitensis var. melitensis was isolated from blood cultures at this time. The patient's temperature did not rise above 38.3 C. (100.9 F.). On May 11 a transfusion of 500 cc. of blood was given, the donor of which had Brucella agglutinins in high titer. On the following day the patient became afebrile and sulfapyridine, refused by the patient for the preceding two days, was resumed. The oral lesions disappeared in eight days and progressive diminution

in the size of the lymph nodes was noted. Blood cultures became sterile and the patient was discharged much improved on May 21. Sulfapyridine was continued for five days.

The patient returned on June 20 complaining of weakness and severe pruritus. It was thought that there had been an increase in the size of the cervical and left axillary nodes. She was readmitted to the hospital July 18, complaining of further enlargement of the lymph nodes, severe pruritus and weakness. She had had no known fever, and no loss of weight had occurred. For the preceding two weeks she had had a nonproductive, paroxysmal cough when lying on her back and a feeling of "tightness" on swallowing.

The temperature at this time was 37.8 C. (100 F.), pulse 80 and respiratory rate 20. The patient appeared chronically ill. Numerous discrete, firm, nontender lymph nodes from 1 to 2 cm. in diameter filled the left anterior and posterior cervical regions. Single nodes of similar size were felt in the submental region and above the suprasternal notch. A few small cervical nodes were felt on the right. In the left axilla a large mass of variously sized nodes measured 8 by 8 cm. The right axillary, epitrochlear and inguinal nodes were slightly enlarged. Examination of the heart and lungs was not remarkable. The firm, nontender liver edge was felt 3 cm. below the costal margin; the spleen was not felt.

A blood count revealed hemoglobin 72 per cent, red blood cells 3,320,000, white blood cells 18,800, polymorphonuclears 88 per cent (stab cells 11 per cent, juveniles 1 per cent), eosinophils 1 per cent, basophils 0, large lymphocytes 2 per cent, small lymphocytes 5 per cent and monocytes 4 per cent. A roentgenogram of the chest showed extensive mediastinal and hilar enlargement. Biopsy of a cervical node showed the characteristic signs of Hodgkin's disease; cultures of the node were sterile. Biopsy of the skin showed no definite lesions.

During the first week of the patient's hospital stay there was a daily elevation of temperature to 38.6 C. (101.5 F.), thereafter to 39.4 C. (102.9 F.). On July 22 sulfapyridine was started but had to be discontinued because of nausea and vomiting. Fifty cc. of bovine antimelitensis serum was given intravenously on August 2. On August 3 roentgen therapy to the cervical, mediastinal and upper abdominal regions was started. Her condition was unchanged at the time of discharge on August 10, but subsequently there was a marked decrease in the size of the cervical nodes and subsidence of cough.

The patient has returned for reexamination at intervals of from four to six weeks. Superficial enlargement of the lymph nodes and mediastinal enlargement have been recurrent, and areas of infiltration into the lungs have been demonstrable roentgenologically. Intermittent fever, cough and fatigability have continued. Under roentgen therapy there has been slight temporary improvement in her general condition.

This case is of interest because of the long duration of the disease with a tendency toward localization of the involvement of the lymph nodes. A clinical picture developed indistinguishable from acute brucellosis, and Brucella melitensis var. melitensis was isolated from blood and oral lesions. Coincidentally there were further enlargement of the lymph nodes and intensified pruritus. Although the stomatitis cleared and blood cultures became negative under treatment with sulfapyridine and immunotransfusion, the patient's general condition became worse and there was rapid and widespread progression of the Hodgkin's disease process.

CASE 8.—*Cervical lymph node enlargement of two years' duration; isolation of Brucella melitensis var. suis from blood and lymph node cultures; treatment with sulfapyridine and immune serum; death three years after onset.*

E. D., a Negro boy aged 6 years, was brought to the hospital on April 26, 1938, because of swelling in the right side of the neck of two years' duration. This enlargement of the neck was progressive and associated with intermittent fever of unknown degree. Several weeks before entry increasing weakness, palpitation and shortness of breath developed.

On physical examination the temperature was 39 C. (102 F.), pulse rate 120 and respiratory rate 28. The patient was weak and undernourished but in no acute distress. An enormous S shaped mass filled the entire right cervical region extending 25 cm. from below the ear over the clavicle and onto the shoulder and anterior wall of the chest. This mass was composed of firm, nontender lymph nodes measuring up to 5 cm. in diameter. A similar mass was felt in the left supraclavicular region, measuring about 8 cm. in diameter. There was no other lymph node enlargement. Examination of the chest was not remarkable. The liver was not palpable. The spleen was felt 5 cm. below the costal margin. There was slight edema of the ankles.

The Wassermann and Kahn reactions of the blood were negative; a blood count revealed hemoglobin 29 per cent, red blood cells 1,840,000, white blood cells 3,480, polymorphonuclears 74 per cent, eosinophils 1 per cent, large lymphocytes 4 per cent, small lymphocytes 13 per cent, monocytes 8 per cent. A roentgenogram of the chest showed marked tracheal displacement and a diffuse shadow extending out into the upper portion of the left lung field which could not be differentiated from displacement of the aorta. The enlarged mass in the neck obscured the right upper and middle lung fields. Biopsy of a cervical lymph node showed the histopathologic picture of Hodgkin's disease. Brucella melitensis var. suis was isolated

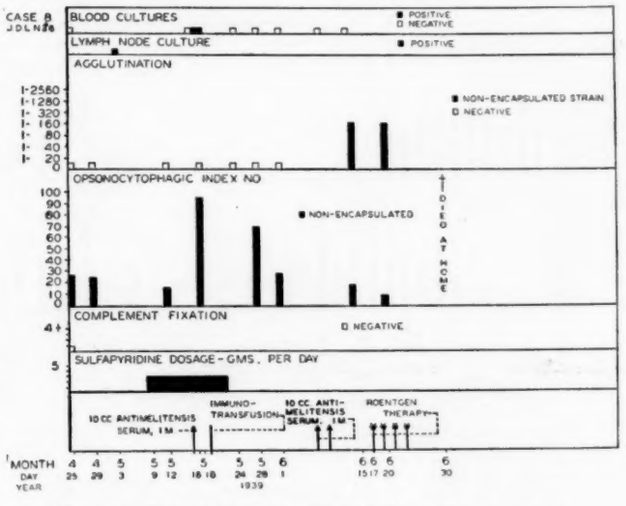


Chart 5.—Bacteriologic and immunologic studies in case 8.

from this node and from the blood. Immunologic studies are given in chart 5.

During the first four weeks of the patient's stay in the hospital there was irregular fever reaching 40.1 C. (104.2 F.). Repeated blood transfusions were given. Sulfapyridine was started on May 9 and discontinued on May 22 because of increasing leukopenia. Ten cc. of bovine antimelitensis serum was given intramuscularly on May 16. On May 19, following a blood transfusion from a donor found to have evidence of immunity to Brucella infection, the patient's temperature fell promptly and after remaining within normal limits for six days rose again. By May 25 a marked decrease in the size of the enlarged lymph nodes had occurred. Repeated injections of bovine antimelitensis serum on June 6 and June 8 were without demonstrable effect. Roentgen therapy to the cervical and mediastinal regions was started on June 17, resulting in a gradual diminution of fever but without further reduction in the size of the enlarged nodes. The patient appeared to be improved when discharged from the hospital on June 27 but he died quietly at home on June 30, 1939. Permission for necropsy was not obtained.

Treatment with sulfapyridine and immune serum apparently caused a marked reduction in the size of this patient's tremendously enlarged lymph nodes. There was no significant immune response to the Brucella infection.

CASE 9.—*Intermittent fever; enlargement of the cervical and axillary lymph nodes on the left and hepatomegaly of three months' duration; Brucella melitensis var. melitensis isolated from blood cultures; treatment with sulfapyridine; recurrence of fever with icterus; treatment with antimelitensis serum; death one year after onset.*

P. W., a man aged 29, a mulatto, admitted to the hospital on May 23, 1939, complained of weakness and swelling of the neck of three months' duration. His illness was considered to have started in the spring of 1939 with a gradual onset of anorexia, malaise, loss of weight and the appearance of painless swellings in the left side of the neck and in both axillas. There had been occasional bouts of high fever and recurrent generalized abdominal discomfort with dull aching pain in the lumbar region.

The temperature was 37.1 C. (98.8 F.), pulse 100, respiratory rate 20 and blood pressure 120 systolic and 70 diastolic. The patient was poorly nourished and appeared chronically ill. On the left side of the neck and in the left axilla there were large, firm, movable, nontender masses of lymph nodes measuring 5 by 3 cm. There was no other lymph node enlargement. Examination of the abdomen revealed marked voluntary muscle spasm. The liver extended 8 cm. below the right costal margin and was firm and tender. The spleen was not felt.

Wassermann and Kahn reactions were negative; a blood count revealed hemoglobin 52 per cent, red blood cells 3,490,000, white blood cells 6,700, polymorphonuclears 85 per cent (stab cells 23 per cent), eosinophils 0, basophils 0, large lymphocytes 2 per cent, small lymphocytes 4 per cent, monocytes 9 per cent. A roentgenogram of the chest showed moderately dense masses at the pulmonary hili which were considered to be enlarged lymph nodes. Bacteriologic and immunologic studies are given in chart 6.

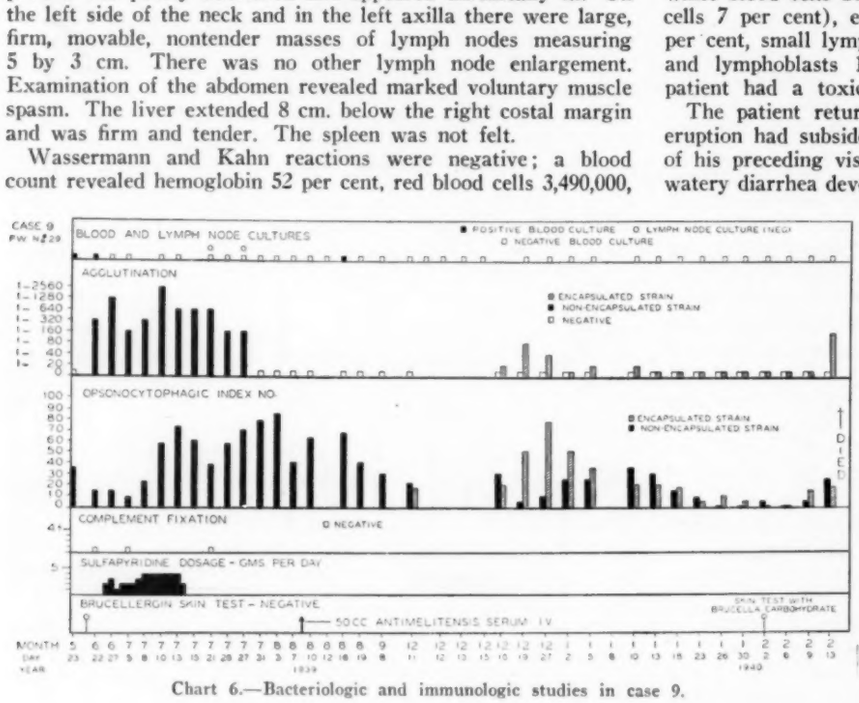


Chart 6.—Bacteriologic and immunologic studies in case 9.

The patient returned May 30, saying that he had had a mild infection of the upper respiratory tract and believed that he had had intermittent fever. The temperature was 39.7 C. (103.4 F.), pulse 112, respiratory rate 24. There was no significant change in the physical examination.

He was admitted to the hospital on June 21. In the interval he had continued to have intermittent fever, malaise and progressive loss of weight.

The temperature was 37.4 C. (99.3 F.), pulse 86, respiratory rate 20 and blood pressure 118 systolic and 74 diastolic. There was no change in the physical condition except for marked enlargement of the right axillary lymph nodes.

A blood count revealed hemoglobin 73 per cent, red blood cells 3,920,000, white blood cells 8,200, polymorphonuclears 79 per cent (stab cells 7 per cent), eosinphils 0, basophils 1 per cent, large lymphocytes 6 per cent, small lymphocytes 12 per cent, monocytes 2 per cent. A roentgenogram of the chest showed no change. A roentgenogram of the abdomen showed that the liver extended to the iliac crest. Biopsy of a cervical node revealed the histopathologic changes of Hodgkin's disease; node cultures were sterile.

Sulfapyridine was started on June 24 and continued throughout the patient's hospital stay. Three days later the patient's temperature, previously within normal limits, rose to 40.2 C. (104.3 F.). The patient was febrile for seven days, after which his temperature fell by lysis. Coincident with the fall in temperature there was marked diminution in the size of the enlarged lymph nodes and liver and general improvement in the patient's clinical condition. He was much improved when discharged from the hospital on July 15.

He returned on July 21 complaining of a cutaneous eruption. Four days previously he had noticed a generalized erythematous eruption and pustular lesions in the region of the beard. The temperature was 37.5 C. (99.5 F.). There was a pustular eruption in the beard area and a generalized erythematous eruption with ecchymotic lesions over the distal portions of the extremities. Other physical conditions were unchanged. A blood count revealed hemoglobin 67 per cent, red blood cells 3,120,000, white blood cells 26,200, polymorphonuclears 42 per cent (stab cells 7 per cent), eosinophils 1 per cent, large lymphocytes 7 per cent, small lymphocytes 23 per cent, monocytes 7 per cent and lymphoblasts 19 per cent. It was considered that the patient had a toxic erythema due probably to sulfapyridine.

The patient returned on July 26 saying that the cutaneous eruption had subsided rapidly. But on the evening of the day of his preceding visit generalized abdominal pain and a severe watery diarrhea developed. He had had fever and slight nausea. He vomited the morning of the day before admission and a dull, aching pain and extreme soreness in the right upper quadrant developed.

The temperature was 39.8 C. (103.6 F.), pulse rate 120 and respiratory rate 22. The scleras were slightly icteric. A few small, firm lymph nodes were felt in the cervical and left axillary regions. In the right axilla there was a large mass of recently enlarged nodes, each about 1 cm. in diameter. No epitrochlear nodes were felt. The inguinal nodes were barely palpable. The heart and lungs were not remarkable. There was rigidity, exquisite tenderness and rebound tenderness in the right upper quadrant of the abdomen. Elsewhere there was no muscle spasm or tenderness. The liver could not be palpated because of muscular rigidity. The spleen was not felt. No masses were felt. Rectal examination gave negative results. The white blood cells numbered 8,700, polymorphonuclears 74 per cent (stab cells 5 per cent), eosinophils 0, basophils 0, large lymphocytes 5 per cent, small lymphocytes 16 per cent and monocytes 5 per cent. The van den Bergh reaction was direct; serum bilirubin was 3.8 mg. per hundred cubic centimeters.

The condition was considered related to abdominal Hodgkin's disease and the patient was admitted for observation. The day following entry the abdominal signs disappeared. He remained acutely ill with daily elevations of temperature to 40 C. (104 F.) until August 15, at which time he became afebrile and a rapid and marked improvement in his general condition followed. Fifty cc. of bovine antimelitensis serum was given intravenously on August 8. By the time of discharge, August 18, jaundice had disappeared, the enlarged lymph nodes had decreased in size and the spleen and liver were not felt.

The patient was readmitted to the hospital on December 11. In the interval weakness had been progressive and he had had intermittent fever and pain in the right upper quadrant.

The temperature was 38.2 C. (100.7 F.), pulse rate 116 and respiratory rate 30. The patient was pale and extremely emaciated and appeared gravely ill. There was slight icterus of the scleras. The left cervical and axillary nodes were firm, nontender and from 2 to 3 cm. in diameter. Expansion of the chest was poor. Over the right posterior part of the chest there was a palpable and audible friction fremitus with impairment of the percussion note and diminished breath and voice sounds. A systolic murmur was heard over the precordium. The abdomen was distended and the liver dulness extended

to the level of the umbilicus. The spleen was palpable at the costal margin.

A blood count revealed hemoglobin 24 per cent, red blood cells 1,600,000, white blood cells 5,160 with polymorphonuclears 77 per cent (stab cells 5 per cent, juveniles 2 per cent), eosinophils 2 per cent, basophils 0, large lymphocytes 6 per cent, small lymphocytes 7 per cent, monocytes 8 per cent; urine and stool examinations gave negative results; the van den Bergh reaction was direct; plasma bilirubin was 1.4 mg. per hundred cubic centimeters. A roentgenogram of the chest showed the right lung obscured. The patient's course was characterized by fever, reaching 40 C. (104 F.) and progressive cachexia. Treatment was entirely symptomatic. Death occurred on Feb. 14, 1940.

Necropsy showed Hodgkin's disease involving the spleen, liver, adrenals, kidneys, bone marrow and lymph nodes, with compression of the common duct and partial obstruction. From necropsy cultures taken in triplicate Brucella melitensis var. melitensis was isolated from the liver and spleen. Diphtheroids were isolated from a mediastinal node.

Coincident with this patient's initial clinical improvement under sulfapyridine therapy was the appearance of serum agglutinins and increased phagocytosis. Phagocytosis was maintained during a succeeding febrile episode, but all evidence of an immune response was lacking during the terminal phase of the disease.

CASE 10.—C. B., a Negro woman aged 35, who entered the hospital on June 19, 1939, began in January 1939 to have painless, progressive enlargement of the left axillary lymph nodes, malaise and loss of weight. For six weeks preceding entry she had had fever. A firm, nontender, left cervical node, about 2 cm. in diameter, and a left axillary node, about 6 cm. in diameter, were palpable. Biopsy of an axillary node from the left side showed the histopathologic signs of Hodgkin's disease. Cultures taken of the nodes were sterile. Brucella melitensis var. melitensis was isolated from a blood culture taken on entry. The patient was febrile throughout her hospital stay and there was no significant improvement under treatment with sulfapyridine and bovine antimelitensis serum or roentgen therapy. Following discharge on August 12 febrile episodes continued, anemia became marked and death occurred in December. Permission for necropsy was not obtained.

CASE 11.—A. A., a white woman aged 40, admitted to the hospital on June 27, 1939, complained of weakness, loss of weight and enlargement of the neck of seven months' duration. Above the suprasternal notch and in the right cervical region were firm, nontender masses of enlarged lymph nodes measuring 5 by 4 cm. The spleen was palpable at the costal margin. A roentgenogram of the chest showed a large mediastinal mass. Biopsy of a cervical lymph node confirmed the diagnosis of Hodgkin's disease, and culture taken of this node and blood culture yielded Brucella melitensis var. suis. There was a moderate decrease in the size of the cervical and mediastinal lymph nodes under roentgen therapy.

CASE 12.—W. H., a Negro aged 64, admitted to the hospital July 7, 1939, complained of enlargement of the neck of six months' duration. In January 1939 the patient noted a nontender mass beneath the angle of the right jaw. Gradually numerous firm, nontender nodules appeared in both cervical regions which increased to a size sufficient to cause difficulty in rotating the neck. Transient regression of this enlargement had been noted. At the time of entry the anterior and posterior cervical lymph nodes were markedly enlarged, firm and nontender and measured from 1 to 3 cm. in diameter; the epitrochlear and inguinal nodes were barely palpable. Biopsy of a cervical lymph node showed the histopathologic signs of Hodgkin's disease. Cultures of the nodes were sterile. Roentgen therapy was given over the cervical region with prompt regression of enlargement of the lymph nodes, which has not recurred. On October 27, Brucella melitensis var. suis was isolated from a blood culture.

CASE 13.—W. M., a white man aged 37, who entered the hospital Nov. 16, 1939, began to be ill in the summer of 1936 with fatigability, loss of weight and pruritus. In September 1937 painless, slight enlargement of several cervical and inguinal lymph nodes was noted, and biopsy established the diagnosis of Hodgkin's disease. In January 1938 enlargement of cervical, axillary and inguinal lymph nodes was noted and a roentgenogram of the chest showed widening of the mediastinum. Fever was present at this time. Under roentgen therapy the size of the lymph nodes regressed, fever subsided and the patient's general condition improved. There was subsequent recurrent enlargement of various groups of superficial lymph nodes which regressed promptly under roentgen therapy. The patient was relatively well until June 1939, when daily elevation of temperature and marked fatigability became established, but there was no recurrence of enlargement of the lymph nodes. Brucella melitensis var. melitensis was isolated from blood cultures taken on entry to the hospital. Under treatment with sulfanilamide and rabbit antimelitensis serum the patient became afebrile and gained in weight. Subsequently fever returned and a flaccid paralysis of the lower extremities developed with a sensory level at the eighth thoracic segment. Since this time his course has been characterized by fever and progressive cachexia.

CASE 14.—*Intermittent cervical lymph node enlargement regressing under roentgen therapy; hilar lymph node enlargement, fever and development of hepatosplenomegaly with ascites; death seven years after onset; Brucella melitensis var. suis isolated in cultures taken post mortem of liver, spleen and peritoneal fluid.*

G. B., a Jewish boy aged 13 years, who entered the hospital on Jan. 24, 1940, began to be ill in the spring of 1933 with enlargement of a left cervical lymph node, which subsided promptly after roentgen therapy. In July 1933 there had been recurrent enlargement of the lymph nodes in the same region, which again regressed after roentgen therapy but recurred in several months. In April 1936 biopsy of a cervical lymph node showed the histopathologic signs of Hodgkin's disease. The patient had no systemic symptoms until the fall of 1938, when fever, anorexia, marked fatigability and a dull aching pain developed in the upper part of the abdomen. At this time tachycardia, splenic enlargement and slight anemia were noted. In January 1939 a roentgenogram of the chest showed large hilar masses. Roentgen therapy was given over the chest and abdomen with temporary improvement. In July 1939 the patient was given sulfanilamide for one week, during which time the spleen decreased in size and improvement of anemia was noted but weakness continued. In November marked dyspnea developed on exertion with cyanosis and loud wheezing, which subsided after roentgen therapy over the mediastinum and upper part of the abdomen. The liver and spleen were palpable at this time and ascites was slowly accumulating. A daily elevation of temperature to 39 C. (102.2 F.) became established and loss of weight, weakness and anemia increased.

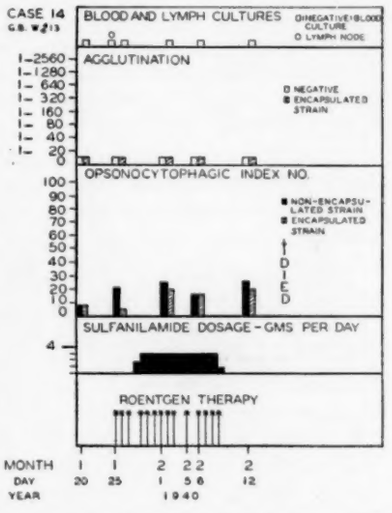


Chart 7.—Bacteriologic and immunologic studies in case 14.

The temperature was 38.1 C. (100.6 F.), the pulse rate 130, respiratory rate 32 and blood pressure 120 systolic, 74 diastolic. The patient was pale and emaciated and appeared chronicaly ill. On the left side single, firm, nontender, cervical and axillary lymph nodes, about 2 cm. in diameter, were felt, as well as many smaller supraclavicular nodes. The inguinal nodes were barely palpable. The chest expanded poorly and there was dulness to flatness posteriorly on the left below the level of the sixth thoracic spine and anteriorly below the level of the fifth rib. The breath and voice sounds were diminished to absent over this area. The heart was enlarged and a systolic murmur was heard over the apex, which was transmitted to

the base. The abdomen was distended and there was shifting dulness in the flanks and a frank fluid wave. The liver edge was felt 9 cm. below the costal margin, firm and nontender. The spleen was felt 14 cm. below the costal margin, firm and moderately tender. Large external hemorrhoids were present. There was slight pitting edema over the dorsum of both feet.

Wassermann and Kahn reactions were negative; hemoglobin was 54 per cent, red blood cells numbered 2,850,000 and white blood cells 7,800, with polymorphonuclears 89 per cent (stab cells 1 per cent), eosinophils 0, basophils 0, large lymphocytes 0, small lymphocytes 5 per cent and monocytes 6 per cent. A roentgenogram of the chest revealed a shadow of uniform density over the lower left lung field and exaggerated hilar markings. Biopsy of a lymph node showed the histopathologic changes of Hodgkin's disease. Cultures taken of the nodes were sterile. Bacteriologic and immunologic studies are given in chart 7.

During the first week in the hospital the patient's temperature varied between 37.6 and 39.9 C. (99.5 and 103.8 F.); thereafter it gradually became lower and did not rise above 38 C. (100.4 F.). Roentgen therapy was given over the spleen, upper part of the abdomen and long bones. Repeated transfusions were given and iron and liver extract were administered, but anemia was progressive. On the fifth hospital day sulfanilamide was started in small doses. The patient became progressively weaker, increasing anemia rapidly developed and death occurred on February 18.

Necropsy showed Hodgkin's disease involving the spleen, liver, diaphragm, pleuras, adrenals and all lymph nodes. Brucella melitensis var. suis and diphtheroids were isolated from triplicate cultures taken of material from the spleen, liver and peritoneal fluid at necropsy. Diphtheroids were also isolated from a mesenteric lymph node.

During the terminal phase of this patient's disease there was no evidence of an immune response toward the Brucella infection which was shown to exist at necropsy.

COMMENT

The demonstration of Brucella infection in fourteen consecutive cases of Hodgkin's disease raises questions that can be answered only by further investigation. The obvious question may be raised as to whether the isolation of this organism from patients with Hodgkin's disease represents merely latent Brucella infection or whether it may be of etiologic significance. It is true that the majority of these fourteen patients were natives of an area in which Brucella infection is widespread, but if our observations represent merely a latent infection peculiar to this region one should expect to obtain positive cultures with equal frequency from lymph nodes obtained from other patients suffering from chronic diseases involving the lymphatic system. Such has not been the case, despite repeated study of a much larger group of patients with diseases such as lymphosarcoma, leukemia, tuberculous adenitis and the like. Brucella has been isolated only once from cultures of sixty-seven lymph nodes removed from patients not suffering from Hodgkin's disease.[2] From such patients repeated blood cultures have been negative with one exception. On the other hand, Brucella has been isolated from blood or lymph nodes on culture, or from both, in these fourteen consecutive cases of Hodgkin's disease. Furthermore, cultures yielding Brucella have been obtained with the greatest frequency when Hodgkin's disease was actively progressing, rather than when it was subacute or temporarily arrested.

A sufficient correlation has been found to exist between the cultural and immunologic manifestations and the clinical course of these patients to justify the belief that the Brucella infection directly influences the syndrome of Hodgkin's disease. The frequent lack of all evidence of an immune response when Brucella could be isolated from blood cultures during recurrences of Hodgkin's disease has been very striking. Maximum clinical improvement in these fourteen cases has coincided with the presence of serum agglutinins and significant degrees of phagocytosis for Brucella.

Although the observations reported here suggest the possible etiologic importance of Brucella in the Hodgkin's disease process, the rigid postulates of Koch have not been fulfilled. It has been possible to induce disease leading to death in guinea pigs and mice by intraperitoneal injection of blood or by a suspension of lymph nodes from patients with Hodgkin's disease and to recover Brucella subsequently from the blood or tissues of these animals, but lesions identical with those of Hodgkin's disease have not been observed. This phase of the problem is being investigated by the department of pathology and will be reported on later.

Treatment of these fourteen patients has been directed primarily toward the existing Brucella infection as a further means of studying the influence of such infection on the course of Hodgkin's disease. A definite and often striking decrease in the size of enlarged lymph nodes has been observed after administration of sulfanilamide or sulfapyridine. Immune serum therapy, utilizing whole blood or blood serum from persons recovered from brucellosis or having serum agglutinins in high titer, or a commercial antiserum, has been combined with sulfanilamide or sulfapyridine, but the effectiveness of these serums has not been demonstrated. Since recent investigations in this laboratory have shown that Brucella organisms isolated from many of the patients suffering from Hodgkin's disease possess capsules and show significant antigenic differences from the laboratory strains, further consideration must be given to the antibody properties of the serums used in the treatment of Brucella infections.

SUMMARY

The coexistence of Brucella infection and Hodgkin's disease has been demonstrated in fourteen consecutive cases by the isolation of Brucella melitensis from blood or lymph node cultures. Brucella has been isolated but once from blood or lymph node cultures from a much larger group suffering from diseases involving the lymph nodes other than those with Hodgkin's disease. Although the data in this study do not establish an etiologic relationship of Brucella to Hodgkin's disease, it is suggested that the clinical course of Hodgkin's disease may be significantly influenced by Brucella infection.

Circumventing Our Conflicts.—It may be profitable to examine briefly a few of the devices we tend to employ for the purpose of circumventing our conflicts. . . . Projection is a psychological expedient that seeks to circumvent the hard realities of our conflicts by shifting the blame we should accept ourselves upon others or upon the conditions of life. Projection is common, and in its milder exhibitions it is harmless enough. For instance, the batter strikes out, throws down his bat, and says that the umpire needs glasses; the college girl says that the professor must have looked over the papers very hastily or she would have been credited with a perfect paper; the housewife complains that the baking powder was inferior in quality or the biscuits would have risen. But if practiced too frequently and with too much facility, projection readily becomes a grave menace to the integrity of the personality and the peace of the mind. Soon it erects an impassable barrier between the individual and the possibility of seeing himself as he really is. The descent may be very rapid—excessive criticism, pessimism, sarcasm, cynicisim, prejudice, intolerance, hatreds, brooding. And from here it is not a very long step into the territory of mental disease—ideas of reference, hallucinations, delusions of persecution.—Strecker, Edward A., The Man and the Mob, *Mental Hygiene* **24**:529 (Oct.) 1940.

DIFFERENTIAL DIAGNOSIS OF VARIOUS FORMS OF ENCEPHALITIS

JOHN A. TOOMEY, M.D.

CLEVELAND

Sleeping sickness is not the only type of encephalitis. There are many other encephalitides, complexes which are not easily differentiated from one another, complexes which result from a combination of degenerative and disseminated inflammatory changes in the brain, spinal cord and meninges. The lesions of encephalitis are sometimes spotty and scattered, and sometimes generalized. At times the spread of the disease in the central nervous system may be slow and at other times rapid. Therefore diverse signs and symptoms are seen. An encephalitic condition may even have different stages, each stage presenting its own signs, signs which may be referable to the motor, sensory, reflex or autonomic systems and, from an anatomic standpoint, present cerebral, basal ganglionic, bulbar, spinal or meningeal symptoms.

CLASSIFICATION OF ENCEPHALITIDES

A. Encephalitides which occur secondary to or accompany some acute infection:

1. Cerebrospinal fever, chickenpox, dysentery, bacterial endocarditis, herpes zoster, malaria, measles, German measles, mumps, pneumonia, purpura, scarlet fever, puerperal sepsis, smallpox, syphilis, tonsillitis, tuberculosis, typhoid, typhus, undulant fever, whooping cough and any infectious disease of the brain.

2. Usually these include the hemorrhagic types of encephalitis.

B. Encephalitides which occur secondary to ingestion or injections of alcohol, benzene, carbon monoxide, arsenic, lead, thallium, bismuth and so on.

C. Encephalitides associated with poisonings.

D. Encephalitides, toxic neuropathies or encephalopathies (other than those following specific infections) (other synonyms: diffuse meningo-encephalomyelitis, multiple neuritis, toxic neuronitis, acute disseminated encephalomyelitis, dissociated encephalitis), possibly acute multiple sclerosis.

E. Encephalitides which accompany metabolic disorders, such as uremia and the toxemia of pregnancy.

F. Encephalitides associated with localized swellings inside the brain case, probably pressure or irritative phenomena: pachymeningitis, extradural abscess, fractures, and so on.

G. Encephalitides following injection of an active or passive immune principle: smallpox vaccine, rabies vaccine, antitoxins or antiserums (tetanus, diphtheria).

H. Encephalitides caused by specific viruses (other than herpes zoster): Japanese type B encephalitis, St. Louis encephalitis, equine encephalomyelitis, possibly lethargic encephalitis, Australian X disease, polioencephalomyelitis, benign lymphocytic choriomeningitis.

I. Diseases or conditions which simulate encephalitis: caisson disease, convulsions, oculomotor lesions, purulent meningitis, neuroses, acute chorea and vascular lesions in the brain associated with embolus, thrombus or hemorrhage.

From the Department of Pediatrics, Western Reserve University School of Medicine, and the Division of Contagious Diseases, City Hospital.

Read in the panel discussion on Some Contagious Diseases before the Section on Pediatrics at the Ninety-First Annual Session of the American Medical Association, New York, June 13, 1940.

DIFFERENTIAL DIAGNOSIS

A. Most of these clinical conditions are easily recognized from the history. Those that are difficult to differentiate at times are St. Louis encephalitis, equine encephalomyelitis, Japanese type B encephalitis, polioencephalomyelitis, lethargic encephalitis, acute benign lymphocytic choriomeningitis, Australian X disease, Schilder's disease (sometimes), disseminated encephalomyelitis (or toxic neuronitis), acute multiple sclerosis as well as tuberculous and syphilitic meningitis. Some of these diseases are new to most physicians; some have appeared only in certain places, yet experience indicates that such localizations are never permanent and all physicians should be conscious of their existence.

B. Differential diagnosis is based on a consideration of (1) appearance, age, sex and fate of the patient; (2) temperature, pulse and respiratory rate; (3) history of the illness, especially as regards onset and chronology of symptoms; (4) neurologic changes; (5) spinal fluid manifestations; (6) results of immunologic tests in animals.

C. There are various types of lesions. Encephalitis usually involves the upper motor neuron; when this occurs, the signs are hyperactive deep tendon reflexes, loss of superficial abdominal reflexes, presence of pathologic reflexes (Babinski, Oppenheim, Chaddock, Stone), spasticity, incoordination of muscles without loss of function, and a normal electrical reaction. Some patients may have one, some all and some none of these signs, despite the fact that the upper motor neuron is usually irritated. Often the signs are absent, and coma and a condition tantamount to cord shock with generalized flaccidity occur. The encephalitic condition may be combined with signs of a lower motor neuron lesion such as flaccidity, diminished reflexes, loss of motor function, atrophy or reaction to degeneration, or a meningeal type of reaction may be produced with a positive Kernig and Brudzinski sign, stiff neck, opisthotonos and hyperactive reflexes.

1. Appearance, age, sex and fate of the patient: The appearance is not indicative, since any type of encephalitis may produce somnolence, choreiform movements, myoclonic spasms or tics. The swiftness and diffuseness of the spread will determine the appearance of the patient when he is first examined. In polioencephalomyelitis there is usually not much lethargy and the encephalitis does not persist long. In tuberculous meningitis the patient is apathetic at first and only after days of illness does he become somnolent and have choreiform or myoclonic movements. In benign lymphocytic choriomeningitis the patient is active. In St. Louis encephalitis he looks extremely ill and may appear somnolent unless the attack is an abortive one, in which case there may be no objective response. The same general remarks hold true for equine encephalomyelitis. Patients ill with Japanese type B encephalitis and Australian X disease may be apathetic or comatose. Patients ill with lethargic encephalitis may look irritable, stuporous or lethargic. Usually but few symptoms accompany the onset of Schilder's disease. Patients ill with disseminated encephalomyelitis and acute multiple sclerosis are usually mentally fit. In syphilitic meningitis the patients, who are usually in the older age groups, may or may not appear ill.

Equine encephalomyelitis, polioencephalomyelitis and Schilder's disease are more apt to occur in children. Fifty per cent of the cases of Australian X disease occur in children under 5 years of age. Japanese type B

and lethargic encephalitis usually are found in older age groups.

More males than females have Australian X disease, and twice as many males as females have Schilder's disease. Tuberculous meningitis occurs in any sex and at any age, most commonly, however, in childhood.

Lethargic encephalitis comes on in the winter and spring time; polioencephalomyelitis, St. Louis encephalitis, Japanese type B encephalitis and Australian X disease in the summer and early fall. (Australian X disease occurs during the summer months in the Southern hemisphere.) Tuberculous meningitis will happen during any season.

There may be a history of exposure in tuberculous meningitis and a history of an animal epizootic disease in equine encephalomyelitis. The locale suggests the diagnosis of Australian X, Japanese type B and St. Louis encephalitis.

Only rarely does a patient ill with tuberculous meningitis live; for practical purposes it can be said that the mortality rate is 100 per cent. Patients with benign lymphocytic choriomeningitis recover. The mortality in St. Louis encephalitis ranges from 17 to 22 per cent; in children under 15 years it is 5 per cent. In equine encephalomyelitis, 66 per cent die. Cerebral irritation caused by poliomyelitis virus is not serious. It is only when this irritation is combined with a bulbar type of palsy that the mortality rises to from 50 to 90 per cent. From 25 to 40 per cent of those ill with lethargic encephalomyelitis die; in Japanese type B encephalitis, 60 per cent or more die; in Schilder's disease, 100 per cent die, death occurring suddenly or eventually as long as ten to twelve years after the initial onset.

2. Temperature, pulse, respiratory rate: Nothing is distinctive about the temperature reactions, although in tuberculous meningitis there may not be any fever until after the patient has lapsed into somnolence.

A change in the character of the pulse usually depends on the amount of fever, but it may also be influenced by increased pressure on the structures at the base of the brain or by inflammatory involvement of the vagus. Infiltration of the vagus and sixth nerves can be demonstrated in tuberculous meningitis. Biot's type of respiration, alternating apnea and hyperpnea may be produced by increased pressure. When the vagal nerve nuclei are involved, as they are in bulbar polioencephalomyelitis, vagus escapement is the result and a tachycardia together with a slowed but deepened respiratory rate

TABLE 1.—*General Information*

Type of Disease	Age	Sex	Time	Locale	Mortality
Benign lymphocytic choriomeningitis	Any	Any	Any	Any	0
St. Louis encephalitis	Any	Any	Summer	In and near vicinity of St. Louis; along streams?	20%
Equine encephalomyelitis	Children mostly	Any	Summer	Where epizootic diseases occur in animals	70%
Japanese type B encephalitis	Older people	Any	Summer	Japan	60%
Polioencephalomyelitis	Children especially	Any	Summer	Any	70% with bulbar; 0-3% without
Lethargic encephalitis	3d-4th decade	Any	Winter and spring	Any	25-40%
Tuberculous meningitis	Young usually	Any	Any	Any with history of exposure	100%
Syphilitic meningitis	Usually older	Any	Any	Any	30%
Schilder's disease	Young usually	More males	Any	Any	100% eventually
Australian X disease	50% under 5 years of age	More males	Summer	Australia	70%
Acute disseminated encephalomyelitis and acute multiple sclerosis	Any	Any	Any	Any	10%

TABLE 2.—*General Information Continued*

Type of Disease	Temperature	Pulse	Respirations	History	
				Onset	Progress
Benign lymphocytic choriomeningitis	High-moderate	Follows temperature	Follows temperature	Abrupt	Rapid
St. Louis encephalitis	High	Follows temperature	Follows temperature	Abrupt to 1-5 days	Rapid, usually
Equine encephalomyelitis	High	Follows temperature	Follows temperature	Abrupt	Rapid
Japanese type B encephalitis	High	Follows temperature	Follows temperature	Abrupt	Rapid
Polioencephalomyelitis	Either high or low	Normal or fast	Normal or slow and deep	Abrupt or camel type	Rap'd, usually
Lethargic encephalitis	Moderate, occasionally high	Follows temperature	Follows temperature	Abrupt	Variable, slow or rapid
Tuberculous meningitis	Normal, then high	Follows temperature	Irregular or Biot's type	Gradual	Rapid at end
Syphilitic meningitis	Normal or slightly increased	Follows temperature	Follows temperature	Abrupt or gradual	Slow
Schilder's disease	Low	Not abnormal	Not abnormal until end	Slow	Variable
Australian X disease	High	Follows temperature	Follows temperature	Abrupt	Rapid
Acute disseminated encephalomyelitis and acute multiple sclerosis	Low or high	Follows temperature	Follows temperature	Abrupt or gradual	Slow or rapid

develops; when there is a marked increase in basilar pressure the pulse may be slowed down.

3. History of illness, onset and chronology of symptoms: An abrupt onset is usually seen in all types of encephalitis save in those associated with tuberculous meningitis and Schilder's disease. The history in syphilitic meningitis is also variable. In tuberculous meningitis the history is almost pathognomonic, relatively asymptomatic at first, gradually progressing to the final tically comatose and hence not very reactive. Late in the course of tuberculous meningitis, any and every type of neurologic reaction may be found. If there is evidence of an upper motor neuron lesion combined with evidence of a lower motor neuron lesion the latter condition is ignored and a diagnosis of an encephalitis is made unless the paralysis or the lower motor neuron type of lesion is segmental in type, in which case poliomyelitis should be diagnosed.

TABLE 3.—*Spinal Fluid Manifestations*

Type of Disease	Color	Cells		Pressure	Organisms	Globulin	Sugar	Chlorides
		Number	Type					
Benign lymphocytic choriomeningitis	Clear to opaque	100 to 3,000	Lymphocyte	+	—	±	—	No significance
St. Louis encephalitis	Clear	50 to 1,000	Lympnocyte	+	—	+	±	No significance
Equine encephalomyelitis	Clear-ground glass	200 to 2,000	Leukocyte	±	—	++++	—	No significance
Japanese type B encephalitis	Clear	100	Lymphocyte	±	—	+	—	No significance
Polioencephalomyelitis	Clear	20 to 1,000	Lymphocyte may be leukocyte at first	±	—	+	—	No significance
Lethargic encephalitis	Clear	100 to 200	Lymphocyte	±	—	+	—	No significance
Tuberculous meningitis	Clear to faintly opaque	30 to 1,000 usually under 100	Lymphocyte may be leukocyte at first	±	+	+++	Decreased	Decreased
Syphilitic meningitis	Clear	Normal to 500	Lymphocyte	±	—	++	—	No significance
Schilder's disease	Clear	Normal	Normal	—	—	—	—	No significance
Australian X disease	Clear	100	Lymphocyte	±	—	+	—	No significance
Acute disseminated encephalomyelitis and acute multiple sclerosis	Clear	Normal or slight increase	Negative or lymphocyte	—	—	+	—	No significance

TABLE 4.—*General Objective Symptoms*

Type of Disease *	Muscle Pain	Upper Motor Neuron Reflexes	Spastic Plegias	Lower Motor Neuron Reflexes	Flaccid Plegias	Meningeal	Somnolent or Drowsy or Comatose	Psychic, Maniacal, Irritable, Memory, Orientation, Attention, Understanding Poor	Myoclonic Movements, Choreiform Movements, Tremors, Twitchings, Irritations, Hyperkinetic	Ocular			Other Cranial Nerves	Vertigo
										Nystagmus	Muscle Paralysis	Optic Nerve Involvement		
Benign lymphocytic choriomeningitis	—	—	—	—	—	+	+	—	—	—	—	—	—	—
St. Louis encephalitis	—	+	+	—	—	+	+	+	+	—	—	—	—?	+
Equine encephalitis	—	+	—	+	+?	±	+	+	+	—?	—?	—	7th	—
Japanese type B encephalitis	—	±	—	—	—	+	+	+	—	—	—	—	—	—
Polioencephalomyelitis	+	—	—	+	+	+	±	—	±	±	±	—	Anyone	—
Lethargic encephalitis	—	+	±	—	±	+	+	+	+	+	+	±	Others	+
Tuberculous meningitis	±	+	+	+	+	+	+	—	±	+	+	±	Others	—
Syphilitic meningitis	—	—	—	—	±	±	±	±	±	±	+	±	±	—
Schilder's disease	+	+	+	—	—	—	—	+	+	—	—	+?	—	—
Australian X disease	—	+	±	—	—	±	+	+	+	—	—	—	±	—
Acute disseminated encephalomyelitis and acute multiple sclerosis	+	±	—	+	+	±	—	—	±	—	±	+	Others	—

* Of course, patients do not appear comatose and maniacal simultaneously. The plus sign merely indicates that such a condition is possible at some time or another. A plus minus sign indicates that the condition may be present, although usually not.

stage over a period of from seven to twenty-one days. Schilder's disease often extends over a long period of time.

4. Neurologic observations: These are not always helpful, since the nervous system reacts only in certain ways, regardless of the stimulus. One should first ascertain whether an upper motor neuron lesion is present. Theoretically an encephalitis patient should have an upper motor neuron response, but many of the encephalitides so shock the patient, especially in equine encephalomyelitis, as to render him somnolent or prac-

Save for infants under 6 months of age, who rarely show objective neurologic phenomena, signs of meningeal irritation are often present with the various encephalitides. In children the only evidence that there may be trouble is when convulsions, high fever, coma and a bulging fontanel are present.

In the acute stages the Queckenstedt maneuver and the eyeground examination are of little practical value in differential diagnosis save in syphilitic meningitis, in which there may be a neuritis and atrophy. The eye muscles are rarely involved in St. Louis encepha-

litis, Australian X disease, Japanese type B encephalitis and lymphocytic choriomeningitis, although vision may be blurred in the latter. The optic muscles are nearly always involved in lethargic encephalitis, eventually always in tuberculous meningitis and at times in polioencephalomyelitis and syphilitic meningitis.

5. Spinal fluid observations: Any acute infection which causes a pyogenic response is ruled out if lymphocytes are found in the spinal fluid. When an abscess is deeply placed in the brain substance, the cellular reaction in the spinal fluid may first be lymphocytic, the type of cell changing to a polymorphonuclear leukocyte as the mass nears the brain surface. When there is an increase in the number of lymphocytes in the spinal fluid, the patient has some one of the encephalitides or tuberculous or syphilitic meningitis. If the spinal fluid contains 40 per cent or more of lymphocytes, the chances are that the true cellular response will eventually be a lymphocytic increase. During the first day or so after the onset of tuberculous meningitis, the cells found may be chiefly polymorphonuclear leukocytes. There is a change, however, within twenty-four

TABLE 5.—*Immunologic Data*

Type of Disease	Isolation of Virus from the Central Nervous System	Neutralization of Virus with Specific Antiserum	Reproduction of Disease in Animals
Benign lymphocytic choriomeningitis	+	+	+
St. Louis encephalitis	+	+	+
Equine encephalomyelitis	+	+	+
Japanese type B encephalitis	+	+	+
Polioencephalomyelitis	+	+	+
Lethargic encephalitis	—	—	—
Tuberculous meningitis	Organisms can be isolated	—	—
Syphilitic meningitis	Wassermann positive	—	—
Schilder's disease	—	—	—
Australian X disease	+	+	+
Acute disseminated encephalomyelitis and acute multiple sclerosis	—	—	—

to forty-eight hours and the cells then become permanently and predominantly lymphocytes. The chances that a lumbar puncture would be done early enough in the disease to catch such a reaction are very slight and by the time the patient has reached the stage of somnolence the cells are practically always lymphocytic in type. The predominant cells in the first stages of equine encephalomyelitis and polioencephalomyelitis may also be polymorphonuclear leukocytes. In the latter instance, these change to lymphocytes within twenty-four to forty-eight hours. The change seems to occur so slowly, however, in equine encephalomyelitis that the patient may die before this happens. If the predominant cells are lymphocytes, as they usually are by the time the practitioner sees them, the patient has one of the diseases under discussion, Schilder's disease, acute multiple sclerosis and disseminated encephalomyelitis excepted.

The total number of cells in the spinal fluid varies. In lethargic encephalitis there may be no cells to a hundred, usually from thirty to fifty; in lymphocytic choriomeningitis, as in equine encephalomyelitis, Japanese type B encephalitis and Australian X disease, there may be as high as a few thousand. In tuberculous meningitis the cell count is low, the average being less than 100, although at times it may be as high as from 500 to 1,000. There is no cellular reaction in Schilder's disease. There may be from a few to a few hundred cells in syphilitic meningitis.

The more protein present in the spinal fluid, the more severe the disease. Compared to the number of cells in lymphocytic choriomeningitis but little protein is found, and that is usually due to nucleoproteins, since filtering out the cells seems to remove it. A relatively small amount is present in lethargic encephalitis, definitely more in equine encephalomyelitis, Japanese type B encephalitis and St. Louis encephalitis, and a goodly quantity in tuberculous meningitis. In acute disseminated encephalomyelitis (and acute multiple sclerosis) there is nearly always a slight or a moderate amount of protein and few or, more often, no cells.

The spinal fluid Wassermann reaction will be positive in syphilitic meningitis and a syphilitic colloidal gold curve produced.

The sugar content is slightly increased in cases of epidemic encephalitis; it is definitely decreased in tuberculous meningitis.

6. Immunologic tests: There are only two ways to identify disease beyond a doubt: (1) by isolating the causative factor in the central nervous system and (2), if the patient recovers, by demonstrating that he has specific neutralizing antibodies in the blood serum. Isolation of the virus factor has occurred in lymphocytic choriomeningitis, St. Louis encephalitis, Japanese type B encephalitis, Australian X disease, equine encephalomyelitis and poliomyelitis. Specific neutralizing antibodies are present in the same diseases. No virus has ever been isolated in lethargic encephalitis, disseminated encephalomyelitis or acute multiple sclerosis.

CONCLUSIONS

If a patient has a disease of sudden onset and a spinal fluid containing but little protein and a great many cells, practically all of which are lymphocytes, and he begins to get well within a few days and there are no sequelae, the diagnosis may be lymphocytic choriomeningitis or abortive poliomyelitis.

If during the summer, in a community where horses, pigeons and other animals are dying of an epizootic disease, a patient develops a disease the onset of which is sudden and explosive in type, accompanied by high fever, not too obvious neurologic symptoms and from 200 to 2,000 cells, practically all polymorphonuclear leukocytes, and no organisms in the spinal fluid, the diagnosis is probably equine encephalomyelitis.

If during the summer a patient has signs similar to those of equine encephalomyelitis but with a lymphocytic count in the spinal fluid, then, dependent on the location, Japanese encephalitis, St. Louis encephalomyelitis or Australian X disease may be considered.

If the patient has a disease with a gradual onset, at first with little or no fever, and he slowly but inexorably becomes worse over a period of from seven to twenty-one days, the disease going on to a somnolent or encephalitic condition, at which time fever appears, and if at this time there are bizarre neurologic signs and an increase in the number of cells in the spinal fluid practically all of which are lymphocytes, the diagnosis is probably tuberculous meningitis. Guinea pig inoculations confirm this as well as demonstrating the presence of the organism.

If during the winter, fall or spring the disease starts suddenly with signs of an upper motor neuron lesion, such as a tic, nystagmus, double vision, absent abdomi-

nal reflexes and hyperactive deep reflexes or even pathologic reflexes, and if the spinal fluid contains some protein and but a slightly increased number of cells, all of which are lymphocytes, the diagnosis is probably lethargic encephalitis.

If the disease starts slowly and extends slowly and the patient shows signs of disturbed vision, spastic paralysis and mental retardation, Schilder's disease should be considered.

If all the signs of an encephalitis appear and yet there are segmental palsies of a lower motor neuron type in the muscles of the arms or legs, the diagnosis is polioencephalomyelitis.

If the patient develops spotty signs of motor and sensory involvement, especially a dissociated appreciation of pain and temperature sensation, and paralysis with bizarre reflex responses, and the spinal fluid contains few or no cells and an increased amount of protein, the patient probably has disseminated encephalomyelitis. Such a syndrome cannot be differentiated from acute multiple sclerosis at this stage. If the patient recovers and has recurrences, multiple sclerosis is thought of; if he remains permanently cured, disseminated encephalomyelitis is considered.

3395 Scranton Road.

Clinical Notes, Suggestions and New Instruments

USE OF CELLOPHANE CYLINDERS FOR DESICCATING BLOOD PLASMA

A RAPID, ECONOMICAL AND BACTERIOLOGICALLY SAFE METHOD

F. W. HARTMAN, M.D., WITH THE ASSISTANCE OF
FRANK W. HARTMAN JR.
DETROIT

The present day use of blood banks and the tendency toward the use of stored blood and blood plasma have emphasized the importance of methods for preserving the plasma. At constant low temperatures liquid plasma may be stored safely for a number of months, but such conditions are difficult and expensive to maintain. Storage of large quantities of liquid under these exacting conditions is best accomplished only in stationary units, so that the mobility necessary for military or other emergency uses presents further expensive obstacles.

As pointed out by Flosdorf and Mudd [1] in 1935, the desiccation of serum was successfully accomplished by C. Martin in 1896, by M. J. Rosenau in 1895, by Noguchi in 1907 and by Burrows and Cohn in 1918. But all these methods produced physicochemical changes in the material and a poorly soluble end product. Shackell in 1909 first introduced the process of desiccation by means of freezing, vacuum and sulfuric acid. Reichel in 1932 improved the method of Shackell and was able to desiccate large quantities rapidly but had difficulty in handling the hydroscopic product.

Flosdorf and Mudd introduced a modification of Shackell's and Reichel's method by processing the serum in the original containers. They (1) secured automatic regulation of the temperature during processing, (2) completed dehydration within a reasonable time, (3) provided a practical means of sealing the containers without loss of vacuum and (4) preserved asepsis throughout the process.

In 1938 Flosdorf and Mudd [2] further improved their method by the addition of a chemical desiccant—anhydrous calcium sulfate, or "drierite"—and designated it the "cryochem-process." Again in 1940 a purely mechanical method of desiccation with a high vacuum or "desivac process" was described by the same authors.[3]

As early as 1917 Phillip A. Kober [4] demonstrated the great speed with which water vapor passed through collodion bags and called the process pervaporation, at the same time describing the process of perstillation and percrystallization, which also utilized collodion bags.

Kunitz and Simms [5] in 1928 and Simms [6] in 1930 described a concentrating dialyzer which consisted of collodion sacs under partial vacuum, using it also to concentrate fluid to small amounts while keeping it at a low temperature.

Morell and Shwartzman [7] in 1937 used small cellophane bags to prepare and preserve bacterial products.

William Thalhimer [8] in 1938 pointed out that cellophane bags could readily be made from cellophane tubing and could be sterilized in steam. He found that bags containing 1,000 cc. of filtered serum could be reduced by from 20 to 25 cc. an hour if suspended at room temperature in front of an electric fan, and almost as fast in the refrigerator. Further, it was pointed out that the concentrated serum could be regenerated by placing the bag in water.

Following the introduction of cellophane tubing as a substitute for rubber tubing in intravenous therapy,[9] we noted the rapid concentration of whole blood hung up in these three-eighths inch diameter tubes with complete desiccation of 150 cc. in twelve hours at 70 F. This led to a review of the literature and further experimentation with lengths of three-eighths inch tubing and with 4½ inch tubing. The initial loss of water vapor from blood plasma from the tubes was rapid, especially when a fan was played on them; but the further the concentration proceeded the slower the process proved, so that from seventy-two to ninety-six hours were required to desiccate 400 cc. of plasma completely. Further, it was noted that in the latter part of the process an abundant gray precipitate was thrown down. The final product was a rubbery opaque mass which was only slowly soluble after being ground in a mortar. Once this product was dissolved, it began precipitating out again so that it was not suitable for intravenous injections into either animals or man.

Flosdorf and Mudd emphasized the rapidity of desiccation and the porous product obtained by their method; efforts to approach their results led us to devise the double walled cellophane cylinders (*E* in the illustration), sealed at each end, thus increasing the surface area 100 per cent and allowing for the circulation of air through the center as well as about the outside. The inner cylinder is made somewhat longer, so that filtered air may be introduced with the plasma. The ends are sealed with heavily tinned screw clamps (*B* and *C*). A metal bar (*D*) is soldered across the outer clamp so that the cylinder may be attached to the rotating mechanism. *F* shows the rotating unit consisting of two wheels, each 24 or more inches in diameter, mounted on a steel axle. Rotation is accomplished at 20 revolutions per minute by means of a small geared motor. Circulation of warm dry air is provided by a 16 inch electric fan (*H*) on which are mounted several electric strip heaters (*G*). On the rotor, which measures 24 inches in diameter, from twelve to eighteen cylinder units (*E*) 14 inches long and 4½ inches in diameter, each containing 300 cc. of plasma, may be attached. Thus 5,400 cc. of plasma may be desiccated at one time with the smallest unit.

The cellophane cylinders of larger size were furnished through the courtesy of the Visking Corporation of Chicago. These cylinders are dry and are thinly coated with glycerin. In the

From the Department of Laboratories, Henry Ford Hospital.

1. Flosdorf, E. W., and Mudd, Stuart: Procedure and Apparatus for Preservation in "Lyophile" Form of Serum and Other Biological Substances, J. Immunology **29:** 389-425 (Nov.) 1935.

2. Flosdorf, E. W., and Mudd, Stuart: An Improved Procedure and Apparatus for Preservation of Sera, Micro-Organisms and Other Substances—the Cryochem-Process, J. Immunology **34:** 469-490 (June) 1938.

3. Flosdorf, E. W.; Stokes, F. J., and Mudd, Stuart: The Desivac Process for Drying from the Frozen State, J. A. M. A. **115:** 1095-1097 (Sept. 28) 1940.

4. Kober, P. A.: Pervaporation, Perstillation and Percrystallization, J. Am. Chem. Soc. **39:** 944-948, 1917.

5. Kunitz, M., and Simms, H. S.: Dialysis with Stirring, J. Gen. Physiol. **11:** 641-644, 1928.

6. Simms, H. S.: A Concentrating Dialyzer, J. Exper. Med. **51:** 319-326 (Feb.) 1930.

7. Morell, Sam, and Shwartzman, Gregory: The Use of Dialysis in the Preparation and Purification of Immunologically Active Bacterial Products, Science **86:** 130 (Aug. 6) 1937.

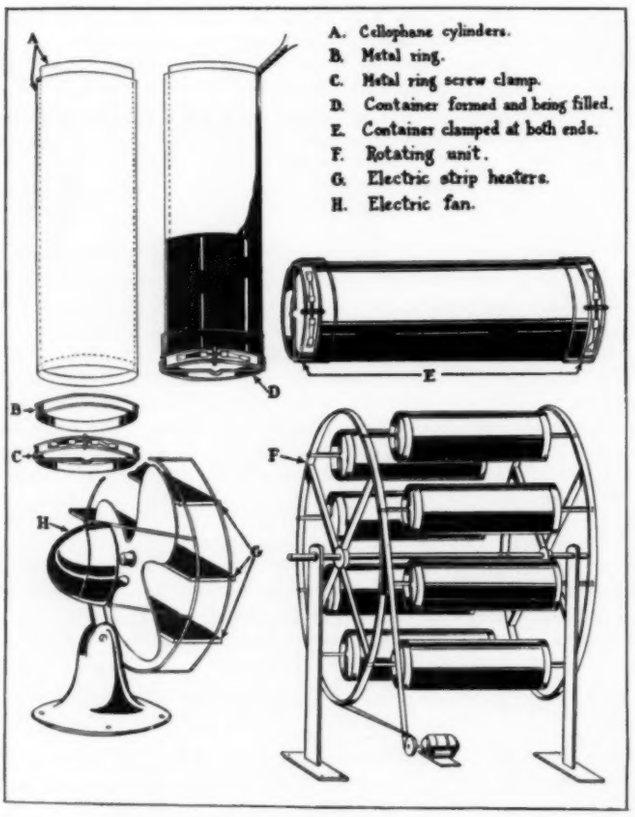
8. Thalhimer, William: A Simple Inexpensive Method for Concentrating Serum Under Sterile Conditions, Soc. Proc. Exper. Biol. & Med. **37:** 639-641 (Jan.) 1938.

9. Hartman, F. W.: The Elimination of Rubber Tubing on Intravenous Sets, Ann. Surg. **111:** 498-501 (March) 1940.

preparation of the cylinders they are washed in distilled water and then boiled in two changes of double distilled water for ten minutes. They are then again thoroughly rinsed with double distilled water. Now the sealing ring is applied at one end and double distilled water is run in to test for leaks. With the second sealing ring the cylinders are placed in a large Petri dish and sterilized with steam for twenty minutes at 30 pounds pressure. The cylinders must be kept moist throughout sterilization and until filled with plasma. Filling is done in a small closed room. The cylinders are separated with sterile forceps and the plasma is pipetted or poured between the inner and the outer cylinder. Then the edges are approximated and air filtered through cotton is introduced. The ends of the two cylinders are folded over twice and the sealing ring is put in place. The filled and sealed container is now attached to the rotor by means of heavy rubber bands.

As the rotation takes place the plasma comes in contact with the entire surface of the inner and outer cellophane cylinders, and mixing with the air produces marked foaming, which increases as the concentration of the plasma proceeds. As a result of the rotation and foaming the residue is desiccated as a light, airy froth which breaks up into porous flakes or crystals. The rate of desiccation of plasma ranged from 60 to 75 cc. an hour in the small cylinders (14 by 4½ inches) and from 130 to 160 cc. an hour in the larger cylinders (22 by 6½ inches).

After desiccation the froth is broken into flakes or crystals by gently working the cellophane cylinders between the fingers or hands. The cylinders are then folded and placed in flat tin boxes of appropriate size, sealed with "scotch" tape.



Apparatus used for desiccating blood plasma.

When the desiccated plasma is to be regenerated the cellophane cylinders are cut cleanly across with flame sterilized scissors or knife and the flakes are poured into the proper amount of sterile distilled water. From two to five minutes of shaking suffices to give a good solution which remains stable for a number of days at 4 C. The solution is usually a light amber and slightly opalescent. The solution is clearer after passage through a Mandler or Seitz filter, but this filtration is unnecessary. The regenerated plasma has been administered to a number of patients without reaction.

In case of an emergency in which distilled water is not available, the desiccated plasma may be regenerated by simply immersing the cylinders in water, as the cellophane is impermeable to bacteria and pyrogens. By rotation, sufficient water is taken up so that a satisfactory though concentrated plasma is obtained in a few hours.

Although the preservation of complement, prothrombin and the like is not considered essential in the desiccation of plasma for intravenous use, since these labile substances are lost for the most part during the storage of the whole blood, we are attempting to preserve these in the cellophane cylinder process by freezing the plasma in a thin layer between the two cylinders, from which the moisture is rapidly extracted without vacuum.

Special Article

GLANDULAR PHYSIOLOGY AND THERAPY

INTRODUCTION

MORRIS FISHBEIN, M.D.
CHICAGO

More than fifteen years have passed since there appeared the first collection of articles on "Glandular Physiology and Therapy," published under the auspices of the Council on Pharmacy and Chemistry of the American Medical Association. Our knowledge has advanced more in these fifteen years than in all the previous centuries of the life of man. So rapid has been the advance that it was necessary to revise the first series in 1927 and the second in 1935. With the passing of the third five-year period, the Council on Pharmacy and Chemistry has considered it desirable again to survey the advancement of our knowledge.

Conspicuous among the reasons for publishing a summary of endocrinology in 1924 was the existence of a pseudoscientific therapy based on glandular materials promoted by pharmaceutical manufacturers with but slight evidence as to actual utility. Much of this empirical and unwarranted therapeusis has disappeared. With the establishment of a new Food and Drug Law and with the coming of the new powers given to the Federal Trade Commission under the Wheeler-Lea Bill, it is likely that still further improvement will occur. The sale of extracts of tonsil, kidney, spleen and heart and, indeed, of mixtures of these with innumerable other preparations, is likely to be better controlled in the future than it has been in the past. No doubt obvious charlatanism will be controlled. However, the difficulty of evaluating therapeutic results and the great psychologic factor involved in most glandular disturbances combine to confuse considerably many physicians who, witnessing the marvels of scientific glandular therapy, are ready to accept as established claims for much that is in no way proved.

The entire volume published in 1927 included only 98 pages. The series issued in 1935 included thirty-one contributions and made a book of 528 pages. In the present series the number of manuscripts is not greatly increased but the amount of material is considerably larger. Particularly important are the articles concerned with the endocrinology of the female reproductive mechanism. Interesting also are those articles which discuss new aspects of our knowledge of the adrenal and the pituitary. Extraordinary advances have been made with reference to the antihormones. Of special importance also are those articles which discuss the interrelationships of various portions of the glandular

apparatus. The investigators who have contributed to this series of articles are all men of note in the fields about which they write.

When the publication of this series of articles in THE JOURNAL is completed, the material will again be made available in book form under the title "Glandular Physiology and Therapy."

RELATIONSHIP OF ANTERIOR LOBE OF THE HYPOPHYSIS TO OTHER ENDOCRINE GLANDS

PHILIP E. SMITH, PH.D.

NEW YORK

This special article is published under the auspices of the Council on Pharmacy and Chemistry. It is one of a series which will be published in book form as the second edition of "Glandular Physiology and Therapy." The opinions expressed in this article are those of the author and do not necessarily represent the views of the Council.—ED.

The laboratory and clinical research which has been carried on since the last edition (1935) of Glandular Physiology and Therapy has not revealed any essentially new interrelationships between the hypophysis and the other glands of internal secretion. Nor have investigations revealed that any of the interrelationships of the hypophysis given in the last edition were erroneous. Important investigations have been reported, however, during this period. Those in the field of carbohydrate and fat metabolism have been especially fruitful. Contributions of preceding years, among which those from the laboratory of Houssay are especially noteworthy, laid the basis for this subsequent extensive work, which has revealed the importance of the interrelationship between the hypophysis and the adrenal cortex in the metabolism of fats and carbohydrates. The results from the work in this field have not yet sufficiently matured to enable one to determine what practical value they will have in clinical medicine, but they contribute greatly to an understanding of the physiology of the hypophysis.

Some advance has been made in the purification of preparations containing the pituitary hormones, though the advances, owing to the protein nature of these hormones, have not kept pace with those made in investigations on the chemically more simple hormones (steroids) of the adrenal gland and the gonads.

Aside from the so-called metabolic principles, five hormones or principles continue to be generally recognized as issuing from the anterior lobe of the hypophysis. These are: (1) the growth (somatotropic) principle; (2) the gonadotropic hormone(s) or complex; (3) the thyrotropic hormone; (4) the corticotropic (adrenotropic) hormone, and (5) the lactogenic hormone.[1] The evidence for the secretion of these separate factors is based on data secured from (1) the effects of hypophysectomy and (2) the effects of the injection of hypophysial extracts in (*a*) animals in which an endocrine deficiency has been established by the ablation of one of the endocrine glands, usually the hypophysis, and (*b*) normal animals.

From the Department of Anatomy, College of Physicians and Surgeons, Columbia University.

1. Other hormones from the hypophysis have been described, but their existence and action are not as well established as the existence and action of the five listed. These other tropic hormones are a medullotropic (Collip) and a pancreatropic hormone (Anselmino, Harold and Hoffman).

EFFECTS OF HYPOPHYSECTOMY

The syndrome from a total deficiency of the anterior lobe of the hypophysis has been studied in all common laboratory animals, in monkeys and in man (Simmonds's disease). The studies are revealing in regard to the relationship of the hypophysis to the other glands of internal secretion and so merit a brief description.

The picture presented after hypophysectomy is quite uniform throughout all species of animals. The thyroid, the adrenal cortex and the gonads and accessory reproductive organs undergo profound involution, and their functional activity is greatly reduced. Parathyroid changes are less definite. Lactation ceases abruptly. The thymus involutes, although this may be an indirect effect. The capacity for muscular work is decreased, and activity is reduced. The appetite is diminished, hypoglycemia of varying degrees of severity develops, the circulation becomes sluggish, and the blood pressure is lowered. In young animals growth ceases abruptly, although very young rats may grow slightly. The viscera are small. Resistance to trauma and infection is greatly diminished, and the basal metabolism is lowered. The resultant effect, then, is atrophy or involution of most of the endocrine glands and polyglandular deficiency. Survival for extensive periods, however, is possible and is dependent to a considerable extent on maintaining the normal food intake and so preventing hypoglycemic coma or convulsions (especially in rabbits and monkeys) and on maintaining normal body temperature. Less care seems to be necessary with rats, ferrets and dogs in order to secure prolonged survival than with other species, including man. It is not probable that even with the greatest care any animal with complete ablation of the anterior lobe of the hypophysis will survive for a normal life span.

A small fragment of functioning gland is able, however, to maintain an animal in an apparently normal condition, and even a fragment of microscopic size has some effect.[2] In rats as little as 10 per cent of the gland will prevent the development of the disabilities, and in monkeys certainly not more than one fourth of the gland is necessary. The hypophysis thus has a great margin of safety, as is true for the other endocrine glands. A fragment which remains appears to have little or no capacity to regenerate, although with regard to this data on monkeys and man are not available.

Experimental work has not sufficed to elucidate the condition of hypofunction in a gland of normal size, for such a condition has not been reported to occur in animals and therefore cannot be studied in them. It is essentially a clinical problem, arising in certain cases from a preponderance of nonsecretory (chromophobe) cells at the expense of secretory (chromophil, i. e., acidophil and basophil) cells.

Experimentally it has been found that a genetic deficiency of one of the two secretory cell types of the anterior lobe of the hypophysis may exist. In the particular strain of mice in which this defect appeared, the acidophils were totally absent, but the chromophobes and basophils were present.[3] The disabilities of hypophysectomy were all present except the atrophy of the genitals, thus supplying additional significant evidence that the basophils elaborate the gonadotropic hormone

2. The literature is reviewed by Smith, P. E., in Allen, Edgar; Danforth, C. H., and Doisy, E. A.: Sex and Internal Secretions, ed. 2, Baltimore, Williams & Wilkins, 1939, p. 391.

3. Smith, P. E., and MacDowell, E. C.: The Differential Effect of Hereditary Mouse Dwarfism on the Anterior Pituitary Hormones, Anat. Rec. **50**: 85 (July 25) 1931.

complex. That a similar condition may occasionally exist in the human subject is indicated in a case recently reported by Shorr and co-workers.[4] The opposite condition, overactivity of a cell type, has long been known from studies on acromegaly, in which there is a tumor of the acidophils.

Experimental and clinical work on the anterior lobe of the hypophysis thus shows that this gland influences, and in most cases directly controls, all of the other glands of internal secretion. These interrelations were all established at the time that the last edition of this book was published, and much of the work since then has been directed toward determining the number of hormones elaborated by the hypophysis and their action and toward the purification of preparations of these hormones.

ACTION OF PITUITARY HORMONES

The Growth Principle.—That the secretion of the hypophysis is essential for general body growth except in the earlier stages of development is unquestionable. The question of the existence of a specific growth-promoting principle would appear to have been raised largely for three reasons: 1. Preparations of the growth-promoting factor have not been free from substances affecting specific organs—thyroid glands, gonads and adrenal glands. 2. Growth is such a complex process, as has been especially pointed out by Stockard,[5] that it is difficult to conceive of its being due to a single hormone. Each of the pituitary tropic hormones is essential for the growth of the specific organ which it affects. 3. The injection of prolactin—a lactogenic factor—causes growth in pigeons and dwarf mice, as shown by Riddle and collaborators.[6] Moreover, in still lower forms (amphibian larvae) the hypophysis can be ablated without inhibiting growth to any great extent.

Specific endocrine stimuli, however, seem to be more necessary for the promotion of growth in mammals than in lower forms, and an interest in comparative physiology should not blind one to the fact that in medical practice the responses of mammals, especially those of man, are of predominant interest. In regard to the contamination of extracts of the growth factor with other anterior pituitary factors, it has been greatly reduced without impairing the growth-stimulating property of the extract.[7] It thus appears, as stated by Evans nearly twenty years ago, that in mammals a specific principle is secreted by the hypophysis which is essential for general body growth. This principle appears to influence skeletal growth mainly by stimulating the epiphysial cartilages, although the effect extends to the soft tissues and the viscera, also.

The Gonadotropic Complex. — The investigations reported by Cushing and collaborators and by Aschner on dogs some thirty years ago revealed that the gonads atrophied after hypophysectomy. Work in 1927 in which atrophic gonads of hypophysectomized rats were repaired and immature ovaries were stimulated to precocious development by administration of pituitary extract gave conclusive proof that there was a factor (or factors) secreted by the hypophysis which was necessary for the structural and functional maintenance of the gonads and through them of the accessory reproductive organs. It was soon discovered, however, that the injection of extracts of hypophyses from different species did not give equal quantitative responses of the different types of tissue composing the gonads. In fact, Evans and Long showed in 1922 that crude extracts of beef hypophyses caused the formation of large amounts of lutein tissue in the ovaries of normal mature rats but had no follicle-stimulating effect. When it was found that the hypophyses of other species—rats, horses, sheep, man—gave pronounced follicle-stimulating effects, indirect evidence was thus supplied that more than one gonadotropic hormone had been encountered.

Fractionation and purification of gonadotropic extracts were undertaken by several investigators (Fevold, Hisaw and Leonard,[8] Wallen-Lawrence,[9] Evans and associates[10]). The present consensus from the laboratories in which these studies are being made is that two gonadotropic principles are elaborated by the anterior lobe of the hypophysis. The determination of the number of gonadotropic hormones is not easy to make, however, and in my opinion has not been definitely made. The length of treatment, the rate of absorption, the dosage and the site of injection (subcutaneous or intraperitoneal) all influence the response. That the solution of the problem is difficult is attested by the fact that within a six year period investigators in one prominent laboratory have stated that there was only one, that there were four and later that there were two pituitary gonadotropic hormones. The two postulated hormones are usually designated as the follicle-stimulating and the luteinizing hormone. The second hormone is sometimes designated as the interstitial cell–stimulating hormone instead of the luteinizer.

The hypophysial luteinizing hormone is not identical with the gonadotropic principle of human pregnancy urine, which is sometimes designated as the luteinizing hormone.[11] Little is known of the chemical composition of the gonadotropic factors, a statement which is also true of the other hypophysial principles.

The Thyrotropic Hormone.—It has been known since the classic work of Rogowitsch in 1889 that the hypophysis is influenced by the thyroid. The determination of an effect of the hypophysis on the thyroid is much more recent. This effect was first demonstrated by hypophysectomy and the injection of hypophysial extracts in amphibia[12] and later in mammals.[13] The

4. Reported at the Annual Meeting of the Association for the Study of Internal Secretions in June 1940.

5. Stockard, C. R.; in discussion on Evans.[7]

6. Bates, R. W.; Riddle, Oscar; Lahr, E. L., and Schooley, J. P.: Aspects of Splanchnomegaly Associated with the Action of Prolactin, Am. J. Physiol. **119**: 603 (July) 1937. Bates, R. W.; Laanes, Theophil, and Riddle, Oscar: Evidence Against the Individuality of the Growth Hormone, Proc. Soc. Exper. Biol. & Med. **33**: 446 (Dec.) 1935.

7. Evans, H. M.: The Hypophyseal Growth Hormone, A. Research Nerv. & Ment. Dis., Proc. (1936) **17**: 175, 1938. Meamber, D. L.; Fraenkel-Conrat, H. L.; Simpson, Miriam E., and Evans, H. M.: The Preparation of Pituitary Growth Hormone Free from Lactogenic and Thyrotropic Hormones, Science **90**: 19 (July 7) 1939.

8. Fevold, H. L.; Hisaw, F. L., and Leonard, S. L.: The Gonad-Stimulating and Luteinizing Hormones of the Anterior Lobe of the Hypophysis, Am. J. Physiol. **97**: 291 (May) 1931. Fevold, H. L.: The Follicle-Stimulating and Luteinizing Hormones of the Anterior Pituitary, in Allen, Edgar; Danforth, C. H., and Doisy, E. A.: Sex and Internal Secretions, Baltimore, Williams & Wilkins Company, 1939, p. 966.

9. Wallen-Lawrence, Zonja: Proof of the Existence of a Follicle-Stimulating and a Luteinizing Hormone in the Anterior Lobe of the Pituitary Body, J. Pharmacol. & Exper. Therap. **51**: 263 (July) 1934.

10. Evans, H. M.; Korpi, Karl; Simpson, Miriam E.; Pencharz, R. I., and Wonder, D. H.: On the Separation of the Interstitial Cell Stimulating, Luteinizing and Follicle Stimulating Fraction in the Anterior Pituitary Gonadotropic Complex, Univ. California Publ. Anat. **1**: 255, 1936.

11. Some commercial descriptive advertisements are misleading in that it is indicated that the hormones from these two sources are identical. All the evidence indicates that the gonadotropic substance in human pregnancy urine is from chorionic tissue, not the hypophysis.

12. The literature is reviewed by P. E. Smith (Relations of the Activity of the Pituitary and Thyroid Glands, in Harvey Lectures, Baltimore, Williams & Wilkins Company, 1930, p. 129).

13. Loeb, L., and Bassett, R. B.: Effect of Hormones of Anterior Pituitary on Thyroid Gland in the Guinea-Pig, Proc. Soc. Exper. Biol. & Med. **26**: 860 (June) 1929. Aron, M.: L'hormone préhypophysaire excito-sécrétrice de la thyroïde, Rev. franç. d'endocrinol. **8**: 472 (Dec.) 1930.

threshold of the stimulus of structural response differs greatly in different species, the thyroids of rats being unchanged in structure by high doses of pituitary thyrotropic extract, whereas the thyroids of guinea pigs and rabbits undergo profound changes even with low doses. The injection of the thyrotropic extract in responsive species results in most of the thyroid changes characteristic of exophthalmic goiter, i. e., increase in size of the thyroid, depletion of iodine, loss of colloid, and hyperplasia and hypertrophy of the cells, with the characteristic irregular type of follicles. The infiltration by lymphocytes and the increase in connective tissue characteristically present in hyperplasia of human thyroids are not present in the hyperplasia experimentally induced. The absence of these changes may be due to the shortness of the period of treatment.

The injection of thyrotropic extract causes also a rapid and marked rise in basal metabolism, although a rise in metabolic rate from pituitary extract has also been reported in thyroidectomized animals.[14] The thyrotropic extract induces a hyperplastic response of thyroid tissue in vitro[15] and also of transplanted thyroids;[16] so it can act independently of any innervation. In man massive doses have been shown to be effective in cases in which hypothyroidism is due to underfunction of the pituitary and not to lack of responsiveness of the thyroid. The thyrotropic extract of pituitary may have a limited field of usefulness, in that its administration will give information as to whether or not hypothyroid states are due to lack of responsiveness of the thyroid to stimulation by the hypophysis. It seems improbable, however, that it can have any extensive clinical usefulness.

The Corticotropic Hormone.—A stimulating action of the anterior lobe of the hypophysis on the adrenal cortex was first shown in amphibia. Hypophysectomy caused profound atrophy of the cortical but not of the medullary component of the adrenal, an action which was confirmed in mammals some ten years later.[17] The atrophy could be prevented or the involuted glands restored to a normal condition by the administration of anterior lobe. There has been much question as to whether or not this cortex-stimulating action of the hypophysis was due to a distinct hormone, but the evidence supplied by Collip and co-workers,[18] Moon[19] and others shows that it is distinct from the thyrotropic, growth-promoting lactogenic and other hypophysial hormones. It appears to have no action other than that of stimulating the cortex of the adrenal.

The injection of a pituitary extract containing the corticotropic factor restores the adrenals after hypophysectomy. It partly restores the work capacity of hypophysectomized animals, although their work capacity still remains somewhat subnormal, as is the case also when cortical extracts are administered.[20]

The injection of cortical extract has been shown to repress the liberation of corticotropic hormone from the hypophysis.[21] It seems probable that the enlargement of the adrenals in normal animals under conditions of stress is due to liberation of unusual amounts of corticotropic hormone by the hypophysis.

As in the case of the thyrotropic extract, it is not probable that the corticotropic extract will prove of much clinical value.

The Lactogenic Hormone.—The pituitary lactogenic hormone (prolactin; galactin; mammotropin) is purely a secretogogue and does not cause development and growth of the mammary glands. It is the only pituitary hormone that has been secured in crystalline form,[22] although the potency of the crystals does not exceed and even may not equal that of the amorphous powder.

The test used for determining lactogenic activity is the response of the crop gland of the pigeon. Riddle has shown that his special preparation, prolactin, has other effects in pigeons, stimulating general body growth and the gastrointestinal tract. These effects are not secured in mammals by the injection of prolactin. Prolactin also stimulates the basal metabolic rate of thyroidectomized pigeons.[23]

The injection of prolactin gives but a temporary increase in milk production in cows,[24] and clinical studies show little or no response following its injection in man.[25]

Relations of the Anterior Lobe of the Hypophysis to Carbohydrate and Fat Metabolism.—The interrelationships of the anterior lobe of the hypophysis and other internal secretory glands in carbohydrate and fat metabolism is a subject which is complex. The reported studies dealing with the injection of pituitary extracts concern themselves largely with "effects" produced by very crude extracts, for the principle or principles producing these effects are in most cases very labile and a degree of purification equal to that achieved with the other pituitary factors has not been obtained. These studies, particularly those of Long and Lukens, have shown an important interrelationship between the hypophysis and the adrenal cortex in carbohydrate metabolism.

Although this complex interrelationship will be discussed more fully in another section, it seems justifiable to discuss briefly some phases of it here. Certain important findings stand out in this work. These are: (1) the greatly increased sensitivity to insulin of hypophysectomized animals, first reported by Houssay and Magenta, in 1924, which was shown later to be due

14. This effect is stated to be due to a specific metabolic principle and not to a tropic hormone (Collip). This principle is remarkably thermostabile and is resistant to boiling in dilute acid and alkali and to peptic digestion. Its injection causes a sharp rise in the metabolic rate for only a few hours. Collip states that it probably has its origin in the pars intermedia but that it is not identical with the melanophore-expanding hormone.

15. Eitel, Hermann; Krebs, H. A., and Loeser, Arnold: Hypophysenvorderlappen und Schilddrüse: Die Wirkung der thyreotropen Substanz des Hypophysenvorderlappens auf die Schilddrüse in vitro, Klin. Wchnschr. **12**: 615 (April 22) 1933.

16. Houssay, B. A.; Biasotti, A., and Magdalena, A.: Hipófisis y tiroides; Acción del extracto del lóbulo anterior de la hipófisis sobre la histología de la tiroides del perro, Rev. Soc. argent. de biol. **8**: 130 (May-June) 1932. Marine, David, and Rosen, S. H.: The Effect of the Thyrotropic Hormone on Auto- and Homeotransplants of the Thyroid and Its Bearing on the Question of Secretory Nerves, Am. J. Physiol. **107**: 677 (March) 1934.

17. Smith, P. E.: The Pigmentary, Growth and Endocrine Disturbances Induced in the Anuran Tadpole by the Early Ablation of the Pars Buccalis of the Hypophysis, in American Anatomical Memoirs, Philadelphia, Wistar Institute of Anatomy and Biology, 1920, No. 11; Hypophysectomy and a Replacement Therapy in the Rat, Am. J. Anat. **45**: 205 (March) 1930.

18. Collip, J. B.; Anderson, E. M., and Thomson, D. L.: Adrenotropic Hormone of Anterior Pituitary Lobe, Lancet **2**: 347 (Aug. 12) 1933.

19. Moon, H. D.: Preparation and Biological Assay of Adrenocorticotropic Hormone, Proc. Soc. Exper. Biol. & Med. **35**: 649 (Jan.) 1937.

20. Ingle, D. J.; Moon, H. D., and Evans, H. M.: Work Performance of Hypophysectomized Rats Treated with Anterior Pituitary Extracts, Am. J. Physiol. **123**: 620 (Sept.) 1938.

21. Ingle, D. J.: The Effects of Administering Large Amounts of Cortin on the Adrenal Cortices of Normal and Hypophysectomized Rats, Am. J. Physiol. **124**: 369 (Nov.) 1938.

22. White, Abraham; Catchpole, H. R., and Long, C. N. H.: Crystalline Protein with High Lactogenic Activity, Science **86**: 82 (July 23) 1937. Shipley, R. A.; Stern, K. G., and White, Abraham: Electrophoresis of Anterior Pituitary Proteins, J. Exper. Med. **69**: 785 (June) 1939.

23. Riddle, Oscar; Smith, G. C.; Bates, R. W.; Moran, C. S., and Lahr, E. L.: Action of Anterior Pituitary Hormones on Basal Metabolism of Normal and Hypophysectomized Pigeons and on the Paradoxical Influence of Temperature, Endocrinology **20**: 1 (Jan.) 1936.

24. Folley, S. J., and Young, F. G.: The Effect of Continued Treatment with Anterior Pituitary Extracts on Milk Volume and Milk-Fat Production in the Lactating Cow, Biochem. J. **33**: 192 (Feb.) 1939.

25. Stewart, H. L., and Pratt, J. B.: Effect of Prolactin on Mammary Gland Secretion, Endocrinology **25**: 347 (Sept.) 1939.

to the loss of the anterior lobe only (Houssay and Potick [26]); (2) the amelioration of experimentally induced diabetes by hypophysectomy, reported by Houssay and Biasotti [27] in 1930 and frequently referred to as "the Houssay phenomenon"; (3) the production of temporary diabetes by injection of anterior pituitary extracts [28] and the production of permanent diabetes by a relatively short course of injections of increasing doses of crude pituitary extracts prepared at low temperatures, reported by Young [29] (diabetogenic effect), in which there is an injury of the islands of Langerhans in the pancreas,[30] with reduction of the pancreatic content of insulin;[31] (4) the amelioration by adrenalectomy of diabetes induced by pancreatectomy, reported by Long and Lukens,[32] and (5) the reinstitution of the diabetic condition by the injection of massive doses of extract of adrenal cortex, reported by Lukens and Dohan.[33] The injection of pituitary extracts causes ketosis in fasting animals.[34] It also will inhibit the action of injected insulin (glycotropic action of Young [35]) and will maintain the levels of muscle glycogen in fasting hypophysectomized animals (glycostatic effect [36]). The rate of absorption of carbohydrates by the intestine, which is decreased by hypophysectomy, can be restored to normal by the administration of thyroid.[37]

It is tempting to ascribe these various metabolic effects to separate hormones but, as emphasized by Long,[38] this is not justifiable with the evidence available.

For the maintenance of diabetes after pancreatectomy, the presence of the adrenal glands has been shown to be essential by Long and Lukens. The ablation of these glands ameliorates the diabetic condition, and although amounts of cortical extract sufficient to maintain the life and health of the experimental animal do not restore the diabetic condition, massive doses will cause recurrence.[39] It appears that the pituitary stimulation of the adrenals, mediated by the corticotropic hormone, is thus essential for the maintenance of the diabetic condition in experimental animals. The opposite condition, hypoglycemia, characteristic of fasting hypophysectomized animals, appears to be attributable, at least in part, to the absence of the stimulating effect of the hypophysis on the adrenals.

Ketosis from the injection of pituitary extract is also dependent on the presence of the adrenals, for this condition is diminished by adrenalectomy.[38] The inhibiting effect of injected pituitary extract on injected insulin (glycotropic action) and the maintenance of muscle glycogen in fasting hypophysectomized animals by the injection of pituitary extract appear to be direct effects, not involving the adrenals.[38]

The inactivation of the thyroid induced by hypophysectomy apparently explains the decreased rate of carbohydrate absorption of pituitaryless animals. Althausen [40] showed that the injection of thyroxin increases the rate of absorption of sugars by the intestine in normal rats, and Russell,[37] following this lead, was able to show that thyroxin restored the normal rate of carbohydrate absorption in hypophysectomized rats. The dose necessary was less than that required for the restoration of the metabolic rate. It thus seems justified to refer the decrease in the rate of absorption of sugars after hypophysectomy to the loss of the thyrotropic hormone and the consequent inactivation of the thyroid.

The observations made in experimental work on the role of the anterior lobe of the pituitary and the interrelationship to other internal secretory glands in carbohydrate and fat metabolism, although of potential importance in medical practice, are not for the most part clinically applicable at present. An exception can perhaps be made with regard to the results of this work relating to the genesis of diabetes mellitus. Although it is generally recognized that many persons with diabetes do not show the islet lesions and thus differ from dogs made permanently diabetic by the injection of pituitary extracts, nevertheless, in other diabetic persons such lesions are present, and it seems not unreasonable to believe that overactivity of the hypophysis was a factor in causing this injury of the islets. As shown by White [41] and others, the incidence of diabetes is higher in children who are unusually tall for their age than it is in those whose growth has not been so rapid, an observation which suggests that increased activity of the hypophysis may be associated with the juvenile onset of this disease. It is also reasonable to assume that there are variations in the susceptibility of the pancreatic islets of different persons to injury. Permanent diabetes does not develop in all dogs from the injection of diabetogenic pituitary extract, and in other species (rats, cats) no injury to the islets results from the injection of such a pituitary extract unless part of the pancreas has been removed.

RECIPROCAL ACTION OF INTERNAL SECRETIONS ON THE HYPOPHYSIS

The functional activity of the hypophysis, i. e., the rate of formation and release of the various pituitary hormones, is influenced by the secretion of the other endocrine glands, so that a balance exists between the various glands. This balance is also influenced by the activity of the other tissues and organs of the body and provides a mechanism which is responsive to the needs of the body. Some examples of the response of

26. Houssay, B. A., and Potick, D.: Antagonisme entre l'hypophyse et l'insuline chez le crapaud, Compt. rend. Soc. de biol. **101**: 940 (July 17) 1929.

27. Houssay, B. A., and Biasotti, A.: Le diabète pancréatique des chiens hypophysectomisés, Compt. rend. Soc. de biol. **105**: 121 (Oct. 16) 1930.

28. Evans, H. M.; Meyer, Karl; Simpson, Miriam E., and Reichert, F. L.: Disturbances of Carbohydrate Metabolism in Normal Dogs Injected with the Hypophyseal Growth Hormone, Proc. Soc. Exper. Biol. & Med. **28**: 857 (April) 1932. Baumann, E. J., and Marine, David: Glycosuria in Rabbits Following Injections of Saline Extract of Anterior Pituitary, ibid. **29**: 1220 (June) 1932.

29. Young, F. G.: Permanent Experimental Diabetes Produced by Pituitary (Anterior Lobe) Injections, Lancet **2**: 372 (Aug. 14) 1937.

30. Richardson, K. C., and Young, F. G.: Histology of Diabetes Induced in Dogs by Injection of Anterior-Pituitary Extracts, Lancet **1**: 1098 (May 14) 1938.

31. Campbell, James, and Best, C. H.: Production of Diabetes in Dogs by Anterior-Pituitary Extracts, Lancet **1**: 1444 (June 25) 1938.

32. Long, C. N. H., and Lukens, F. D. W.: Effects of Adrenalectomy and Hypophysectomy upon Experimental Diabetes in Cat., J. Exper. Med. **63**: 465 (April) 1936.

33. Lukens, F. D. W., and Dohan, F. C.: Further Observations on the Relation of the Adrenal Cortex to Experimental Diabetes, Endocrinology **22**: 51 (Jan.) 1938.

34. Burn, J. H., and Ling, H. W.: Excretion of Acetone Bodies on Fat Diet as Affected by Injection of Pituitary (Anterior Lobe) Extract and by Pregnancy, Quart. J. Pharm. & Pharmacol. **6**: 31 (Jan.-March) 1933.

35. Young, F. G.: The Identity and Mechanism of Action of the Glycotropic (Anti-Insulin) Substance of the Anterior Pitutiary Gland, Biochem. J. **32**: 1521 (Sept.) 1938.

36. Bennett, L. L.: The Interrelation of Pituitary and Adrenal in the Control of Carbohydrate Levels in the Rat, Endocrinology **22**: 193 (Feb.) 1938.

37. Russell, J. A.: The Effect of Thyroxin on the Carbohydrate Metabolism of Hypophysectomized Rats, Am. J. Physiol. **122**: 547 (June) 1938.

38. Long, C. N. H.: Diabetes Mellitus in the Light of Our Present Knowledge of Metabolism, Tr. & Stud., Coll. Physicians, Philadelphia **4**: 21 (April) 1939.

39. Lukens, F. D. W., and Dohan, F. C.: Further Observations on the Relation of the Adrenal Cortex to Experimental Diabetes, Endocrinology **22**: 51 (Jan.) 1938.

40. Althausen, T. L.: Influence of the Thyroid Gland on Intestinal Absorption of Dextrose, Galactose, and Xylose, J. Clin. Investigation **16**: 658 (July) 1937.

41. White, P.: Diabetes in Childhood and Adolescence, Philadelphia, Lea & Febiger, 1932.

the endocrine glands to environmental conditions are the hypertrophy of the adrenal cortex under conditions of stress (cold, toxins, and so on), the hyperplasia of the thyroid of the animal kept in a cold environment, and the enlargement and activation of the gonads in some birds and some mammals, which have a seasonal breeding period, with increased light.[42] Some of the responses, at least, are due to increased activity of the hypophysis. Activation and enlargement of the gonads can be induced in the winter season and in some immature animals by increased illumination. After removal of the eyes, gonad activation can be induced in some birds by direct illumination of the hypophysis through a tube leading to that gland.[43]

Adrenal and Hypophysis.—In a series of papers Ingle [21] has shown that the injection of an extract of adrenal cortex causes a regression of the adrenal cortex which is nearly equal to that resulting from hypophysectomy and that this regression is due to a decrease in the output of corticotropic hormone by the pituitary, for the injection of a corticotropic extract of the pituitary prevented the cortical atrophy. It has been mentioned that the adrenal cortex atrophies after hypophysectomy. In intact animals the cortex hypertrophies under conditions of stress, but in hypophysectomized animals this hypertrophy does not take place. If placed in the cold, the animals thus operated on will succumb at temperatures which will be survived by normal animals or by hypophysectomized animals given an extract of adrenal cortex. Although it cannot be assumed that the adrenal glands are alone responsible for survival with noxious stimuli or under conditions of increased stress, nevertheless they are an important factor in the resistance and survival. The immediate stimulus causing the hypertrophy is the corticotropic secretion of the hypophysis.

Gonads and Hypophysis.—The mechanism operating between the gonads and the hypophysis is similar to that described for the adrenals and the hypophysis. Both clinical and experimental studies show this interrelationship. The fact that the pituitary gonadotropic substance is excreted in man in the urine has given an unexcelled opportunity to study the factors which influence its secretion. The output of gonadotropin in the urine increases in amount if the gonads are removed or undergo involution, as at the menopause. As has been extensively shown by clinical studies, the administration of gonadal products, especially the estrogens, represses this enhanced output. In experimental animals the removal of the gonads results in increased potency of the pituitary, with an increase in the number of basophils. These structural changes can be prevented or the normal structure restored by the injection of estrogen or androgen.

Thyroid and Hypophysis.—Although a structural alteration of the hypophysis from the extirpation of an endocrine gland was first noted from thyroidectomy, and the administration of thyroid alters the proportion and structure of certain of the cell types of the hypophysis, nevertheless a demonstration of the influence of thyroxine on the functional activity of the hypophysis as complete as that in the case of the gonads and adrenals has not been given. The evidence, however, indicates that the output of thyrotropic hormone is repressed by unusual amounts of thyroid secretion. The administration of thyroid causes an involution of this gland, an effect which by analogy with relationships already discussed is presumably due to a decreased output of thyrotropic hormone. Attempts to assay the urinary excretion of the thyrotropic substance have given conflicting results.

In the preceding discussion it has been shown that excessive amounts of the secretion of the gonads, of the cortex of the adrenal and probably also of the thyroid inhibit the corresponding tropic hormones of the hypophysis, thus supplying an important mechanism for the maintenance of a balance between the hypophysis and each of these glands. There is also some evidence that an excessive amount of secretion of one of these glands influences the rate of secretion of the pituitary tropic hormones affecting other glands or structures. The administration of excessive amounts of estrogen promptly inhibits the growth of experimental animals and will inhibit the development of the mammary glands. The administration of thyroid increases the gonadotropic potency of the hypophysis, although the opposite condition, thyroid deficiency, does not reduce the pituitary content of gonad-stimulating hormone. The inhibiting effect of thyroidectomy on growth can be prevented by administering a hypophysial extract containing the growth-promoting factor, so that the inhibition probably is due, in part, to decreased secretion of this growth hormone.

RESPONSIVITY OF ENDOCRINE ORGANS AND OTHER TISSUES TO ENDOCRINE PRODUCTS

It is a fundamental tenet of the concept of internal secretion that the endocrine organs secrete chemical hormones ("messengers") which have specific effects, whether their action is on other endocrine organs, on a tissue group or on all the tissues of the body. This concept, however, does not justify the assumption that a hormone will induce its characteristic effect in all cases. In other words, a capacity of the end organ to respond to a hormone is also essential. Of the many examples which show this, two only will be given. Growth depends not only on the presence of the growth factor but on the responsivity of tissue, as is well shown by results obtained from injections of an extract containing the growth-promoting factor in two races of dogs—dachshund and collie. The injections in the former stimulate primarily a growth in the length of the vertebral column; the injections in the latter, an increase in the length of the legs.[44] There seems to be an inherent, hereditary capacity of response in the vertebral and appendicular components of the skeleton, respectively, in these two strains of dogs. The importance of the growth responsivity of various structures of the body has also been shown by breeding experiments in dogs. Experimental work on the gonads shows that at early ages some of the components of these glands are unresponsive to gonadotropic hormones; responsivity develops with aging. Although the gonadotropic hormones are essential to sexual maturation, it would not be justifiable to attribute sexual maturity solely to the onset of the secretion of these hormones; the development of responsivity to these hormones is also an essential factor. The responsivity of the end organ thus plays an important part in the action and the interrelations of the endocrine glands.

42. The extensive literature is reviewed by M. A. Bissonnette (The Influence of Light upon Pituitary Activity, A. Research Nerv. & Ment. Dis., Proc. [1936] **17**: 361, 1938).

43. Benoit, J.: Etude du mécanisme de la stimulation par la lumière de l'activité testiculaire chez le canard domestique, Bull. biol. **71**: 393, 1937.

44. Evans, H. M.; Meyer, Karl, and Simpson, Miriam E.: The Growth and Gonad-Stimulating Hormones of the Anterior Hypophysis, Memoirs of the University of California, Berkeley, Calif., University of California Press, 1933, vol. 11.

Council on Physical Therapy

THE COUNCIL ON PHYSICAL THERAPY HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORT. HOWARD A. CARTER, Secretary.

DANGERS INCIDENT TO THE INDISCRIMINATE USE OF RADIUM COMPOUNDS OR RADON

IN THE TREATMENT OF CUTANEOUS DISEASES

ANTHONY C. CIPOLLARO, M.D.
NEW YORK

Radium from abroad has found anxious and eager buyers in this country during the past decade. Nine tenths of the radium mined each year finds a use in medicine.[1] The United States is probably the largest consumer of radium and radon for medical purposes, and the decreased cost resulting from a greater supply has made them available for wider distribution.

Formerly American dermatologists received but little instruction in the physical and chemical properties and the uses of radium. With each successive year there has been increased knowledge of the clinical applications of radium and radon. The modern dermatologist utilizes radioactive elements more efficiently than his predecessors and with discriminating judgment.

Notwithstanding increased knowledge, it is regrettable that some physicians, including dermatologists, use radium or radon for the treatment of various dermatoses without having had adequate training of either the disease under treatment or the agent. Some have the fallacious idea that the details of treatment of a lesion requiring irradiation can be obtained from a physicist. Proper treatment of a lesion, no matter how trivial, with an agent so potent as radium or radon requires exact diagnosis and judgment for the selection of the correct dose and technic applicable to the disease. This, of course, means specialized training and knowledge of general dermatology and of that specialized phase of radiology which pertains to dermatology.

The indiscriminate use of radium or radon by an unqualified physician is to be condemned. However, the responsibility also rests with those who sell or rent radium or radon, especially if the medical and physical experts of the distributors give diagnostic aid and suggest treatment without seeing the patient. It is the practice of a few physicians to make a snap diagnosis of a lesion without microscopic confirmation and then seek advice from the radium distributor regarding the dosage, filtration and other technical details. The advice is often given by a physicist or a company physician by mail or over the telephone. Obviously such practice leads to many undesirable results and needless suffering. Because the proper administration of radium treatments requires specialized knowledge, such treatments should be given only by experts who possess complete knowledge of the disease and also of the chemical and physical properties of the therapeutic agent, including dosage measurements. Henry K. Taylor,[2] chairman of the Special Committee on Radiology of the Medical Society of the County of New York, recently stated: "The attention of the committee was called to two radium concerns selling their product by mail with instructions for use. The instructions accompanying the radium were issued by doctors who did not have the privilege of examining the patient. This practice is considered unethical." Other physicians and radiologists have had similar experiences.

It is alleged by some that the curtailment of the widespread distribution and use of radium or radon may deny to some the use of this valuable agent. In my opinion this allegation is not true when it is considered that radium or radon when improperly used can cause damage to the tissues and to the patient that may prove to be far more serious than the original condition. In fact, overtreatment with radium or radon can lead to cancer formation. There are many cases of lupus erythematosus, lupus vulgaris, verruca vulgaris, basal cell epithelioma, naevus vasculosus (port wine marks), psoriasis and sycosis vulgaris in which squamous cell epithelioma developed in active lesions of these diseases or in scars following the involution of these lesions as a result of overtreatment with or indiscriminate use of radium or radon. Therefore, unless radiation is properly used in diseases in which this agent is indicated, it is better not to use it. The mere availability of radium or radon does not compensate for the disastrous results following improper use.

Radium and radon should not be rented or sold to persons who are not qualified to use them, because this practice encourages diagnosis and treatment by mail or telephone by an individual who possesses radium or by a corporation engaged in the sale and rental of radium. There is no way that I know of to stop this practice. However, the dangers following the indiscriminate use of radium or radon can be brought to the attention of the practicing physician. Some steps should be taken toward ending the practice of distributors of radioactive substances giving technical information through a salaried physician or physicist who never sees the patient.

The Council on Physical Therapy desires to acquaint all physicians with the undesirable effects observed when radium and radon are used indiscriminately. This article deals only with the dangers resulting from the improper use of radioactive agents in treating diseases of the skin. The errors usually result from incorrect technic, poor judgment or ignorance.

The dermatologist of today is not the externist he was twenty years ago. He knows much more about the causation and management of many dermatoses. The training in the fundamentals of general medicine and in dermatology in particular is much superior to what it was formerly. Eczema, for example, is divided into several varieties. Identification of the particular variety gives clues as to the cause, proper investigation and therapy. In the case of eczema as in other diseases, irradiation with x-rays or radium was used to relieve symptoms and as a cloak to hide inexact diagnosis, lack of therapeutic resourcefulness, ability and knowledge. Now radiation therapy is used less often because of increased knowledge of the dermatoses. In fact, proper topical therapy, hospitalization, controlled environment and so on will usually produce quicker relief than will x-ray or radium therapy.

The improper treatment of certain diseases with radium, radon or x-rays often leads to irreparable damage to the tissues irradiated. Some of these diseases will be discussed.

Dr. George M. MacKee assisted in the preparation of this paper and gave many valuable suggestions.

From the Skin and Cancer Unit, New York Post-Graduate Medical School and Hospital, Columbia University.

1. Importation of Radium, editorial, J. A. M. A. **112**: 2069 (May 20) 1939.

2. Taylor, Henry K.: Problems of the Special Committee on Radiology, New York M. Week **19**: 4 (July 13) 1940.

CUTANEOUS NEOPLASMS

The physician who treats cutaneous malignant growths should be able to use expertly all the recognized methods of therapy. He should not depend on surgery or irradiation alone. He should be able to use with equal expertness scalpel surgery, electrosurgery, x-rays, radium and radon. The best method or combination of methods should be used for the presenting lesion. The dose of radon, radium or x-rays, the filtration, the distance, the overlapping, the time and other elements should be expertly judged in relation to the size and depth of the lesion, the location, the sex, age and physical condition of the patient and the degree of malignancy. The use of poor judgment in the selection of the proper method of treatment leads to bad results, complications and even death. At this point, I would like to cite an actual case that came to my attention several years ago. An elderly man was treated for a small epithelioma involving the ear with medium voltage and moderately filtered x-rays. It did not respond to the treatment administered and further treatment with x-rays was given. Only a portion of the lesion healed. The remainder was treated with radium. Several months later the lesion had spread and the cartilage and periosteum had been damaged. In addition there were evidences of an acute radiodermatitis. The resistance of the tissues was so lowered that there was also a superimposed eczematous process. Because of this secondary inflammation of the skin, it was impossible to ascertain easily what was dermatitis and what was epithelioma. The pain was so intense that narcotics had to be used for its relief. After the application of soothing remedies, the inflammation subsided. The epithelioma had spread all over the ear, including the external auditory canal and the underlying cartilaginous and bony structures. Extensive surgery was required to ameliorate the condition and reduce the pain. Several years of suffering and convalescence would have been avoided if this patient had been seen by a physician acquainted with all therapeutic methods for such lesions. He would have used a local anesthetic and would have destroyed the entire lesion with electrosurgery or scalpel surgery with plastic repair if necessary. Many other examples of poor results following the improper treatment of cutaneous malignant growths can be cited, but this one case suffices to illustrate the importance of selecting the correct method or combination of methods for the treatment of cancer of the skin.

NEVI

The cavernous and superficial (strawberry) angiomas occurring in children under 1 year of age usually respond well to irradiation. Treatment that may leave x-ray or radium sequelae is contraindicated because many of these lesions may disappear spontaneously. Port wine marks do not respond to irradiation. In fact, many cases which have been treated in the past with radium or radon now show varying degrees of radiodermatitis. No technic now known is safe for the treatment of these lesions. Hairy and nonhairy moles and lymphangiomas respond poorly when treated with radium, radon or x-rays. In fact, any degree of improvement of these lesions is accompanied by a corresponding degree of radiodermatitis.

HYPERTRICHOSIS, HYPERHIDROSIS AND SEBORRHEA

Hundreds of cases of radiodermatitis have been caused by treating hypertrichosis with x-rays and radium. Only a few years ago many beauty parlors were administering x-rays for the treatment of unwanted hairs on any part of the body. In fact, "chain stores" were established throughout the country to administer the so-called Tricho treatment. Many cases of radiodermatitis resulted from the administration of x-rays by untrained lay operators. Fortunately the "Tricho Institute" no longer exists and American women are now sufficiently educated to avoid x-rays or radium for the treatment of superfluous hair. Irradiation is contraindicated for the treatment of this condition regardless of the technic employed and who employs it. Up to the present writing there is no safe radium or x-ray technic for the permanent removal of unwanted hair. Hyperhidrosis and seborrhea may be benefited by irradiation. No more than a safe amount should be given even though there is failure to cure completely. Much harm results in attempting to cure stubborn cases with x-rays or radium when they fail to respond to a safe dose. Attempting to inhibit permanently all secretory activity of the sweat and sebaceous apparatus with radioactive agents may lead to permanent and harmful changes in the surrounding cutaneous structures.

MYCOSIS FUNGOIDES

Mycosis fungoides, a serious disease of the hemopoietic system which often ends fatally, responds exceedingly well to irradiation. As a rule small doses of x-rays or radium administered at weekly intervals to the affected areas causes the lesions to respond. However, when overtreated there may result serious sequelae affecting the skin as well as the blood forming apparatus. Judicious use of the radioactive agents may keep patients with mycosis fungoides free from lesions for many years and may prolong life indefinitely. In fact, many patients with mycosis fungoides die of other diseases. The fungating and ulcerative stage of this disease is seen infrequently now. This is due to the fact that irradiation with x-rays, radium or radon often controls the disease. In the light of our present knowledge it is a mistake to irradiate the bones, spleen and gland bearing areas with large doses of heavily filtered and high voltage x-rays. The disease affects the skin. Radiation applied directly to the affected skin areas in small doses and whenever indicated is all that is required to cause involution of the presenting lesions and to prevent the formation of the fungating and ulcerative lesions.

KELOIDS

Keloids and other benign new growths and hypertrophies and inflammatory dermatoses such as psoriasis or eczema should not be treated with an amount of radiation sufficient to produce erythema, because even one occurrence of a mild erythema may eventuate in disfiguring and even serious sequelae. Failure to cure a benign condition is not so serious as the harmful results which follow the injudicious use of radiation. Keloids are often only of cosmetic importance. Many lesions are radioresistant, especially the older ones. Therefore forcing the issue with x-rays or radium should be avoided. Overdosage may not only fail to improve the condition but may also lead to irreparable skin damage and even to a neoplasm.

Many other diseases might be discussed in detail, but a sufficient number have been mentioned to demonstrate that overtreatment of dermatologic conditions with radiation leads to disastrous consequences.

Radiation therapy is used with more discrimination by the well trained modern dermatologist. The physician who is not a dermatologist is apt to use radium or x-rays when there are better methods. He is apt

to administer a dose which is too large or he may give too many treatments or the intervals between treatments may be too short. In the presence of congestion caused by the disease or inflammation caused by topical remedies (counterirritant ointments or lotions or strong ultraviolet rays) the biologic effect of the radiation is greater than is anticipated. Such congestion or inflammation may mask a slight acute radiodermatitis with resulting unexpected radiation sequelae. Errors are also made in forcing the issue with radiation therapy: If certain cases of eczema, psoriasis and other dermatoses do not respond to an adequate amount of radiation, the continuance of such treatment may lead to therapeutic fastness or radiodermatitis.

Many cases of radiodermatitis and other undesirable radiation reactions result from the improper protection of normal tissue from scattered and secondary radiations. Such areas as the hairy parts, eyes or testes should be protected with suitable opaque materials in all instances. Overdosage may result from crossfiring, back scattering and overlapping of rays. The inadvertent omission of the filter or the improper selection of the filter when administering a radium or x-ray treatment accounts for some cases of radiation sequelae. Radiodermatitis may also result from haphazard guesswork in dosage determination, from faulty diagnosis, from repeated treatment of recurrences and from failure to obtain a history of previous treatments with radium or x-rays. The application of radium or radon over an area that was previously repeatedly examined with x-rays or by fluoroscopy may lead to a radiodermatitis. Perhaps the greatest harm is done with radium by using it when not indicated or as an unnecessary aid to other treatment.

A physician who uses x-rays or radium for treating dermatologic conditions should be a dermatologist or should be guided by one. The necessity for this attitude is best illustrated as follows: A patient may complain of anal pruritus. The diagnosis of essential pruritus ani should be confirmed. Such possible causes as a fungus, diabetes, intestinal parasites, anorectal disorder, allergic conditions or neurodermatitis should be eliminated. If it is assumed that the condition is essential pruritus ani and an adequate amount of irradiation fails to relieve it, then it is unlikely that additional treatment will be effective. The indications, the contraindications, the response of certain diseases to a given quantity of radiation, the tissue response and the natural evolution and involution of dermatoses are best understood by dermatologists. It is also important that the dermatologist who uses radiation be thoroughly familiar with all phases of radiation that apply to the treatment of cutaneous diseases. The details of acute and chronic radiodermatitis may be found in standard textbooks.[3]

I hope that it has been sufficiently emphasized that the proper administration of radium, radon or x-rays in the treatment of cutaneous diseases requires specialized training in both dermatology and radiology. Also that company physicists are not qualified to advise dermatologists or radiologists in the proper use of radium. Especially is it poor practice to obtain advice from company physicians and physicists regarding technic, filtration, dosage, method of administration of radium or radon without the consulting physician or physicist seeing the patient. The practice of telephone and mail consultation is particularly undesirable.

40 East Sixty-First Street.

3. MacKee, George M.: X-Rays and Radium in the Treatment of Diseases of the Skin, Philadelphia, Lea & Febiger, 1939.

Council on Pharmacy and Chemistry

REPORTS OF THE COUNCIL

THE COUNCIL HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORT.

PAUL NICHOLAS LEECH, Secretary.

THE PRESENT STATUS OF THE GONADOTROPIC HORMONE FROM THE SERUM OF PREGNANT MARES: GONADOGEN (THE UPJOHN COMPANY), ANTERON (SCHERING CORPORATION) AND GONADIN (CUTTER LABORATORIES) NOT ACCEPTABLE FOR N. N. R.

The gonadotropin obtained from the serum of pregnant mares is being actively marketed at the present time for therapeutic purposes. The Upjohn Company claims that its preparation of pregnant mares' serum (Gonadogen) is useful in males with hypogonadism of pituitary origin, in oligospermia and sterility, and in females for menstrual irregularities, functional bleeding, certain types of dysmenorrhea, sterility and failure of ovulation.

Schering Corporation recommends Anteron, a similar preparation, in the treatment of amenorrhea, functional bleeding and hypogonadal sterility in females, and sterility and hypogonadism in males.

Gonadin is advertised by Cutter Laboratories to be indicated in amenorrhea, functional bleeding, sterility in the female and disorders of sperm formation in the male.

On theoretical grounds, gonadotropic hormone from serum of pregnant mares appears to possess several desirable physiologic properties which might be enlisted for therapeutic purposes:

1. It is capable of inducing ovarian growth in primates, in contrast to chorionic gonadotropin (from human pregnancy urine), which is unable to affect such ovaries in this regard.
2. It stimulates the germinative epithelium of the ovaries and testes in laboratory animals.
3. Its physiologic properties resemble those of the anterior lobe gonadotropic factors.
4. It can be prepared for commercial purposes in a more concentrated and purer form than gonadotropic extracts of the anterior lobe.

It has been fairly well demonstrated that mare serum gonadotropin is effective in inducing some degree of ovarian growth in human beings. Westman[1] reported that seven women responded with an increased growth of the follicular apparatus, which in five cases he considered excessive. Moricard and Saulnier[2] likewise stimulated follicular development with a similar preparation in several women.

In 1938 Davis and Koff[3] reported that they had induced ovulation in women with the mare serum gonadotropin administered intravenously. No one, up to this time, had succeeded in producing this reaction. The work of these investigators aroused great interest in this preparation, and the application of such therapy to certain gynecologic disorders was held most promising. These authors recognized the possibility, however, that ovulation might be induced in this manner only in women with normal ovaries, which would, of course, limit its therapeutic application. Up to the present time the work of Davis and Koff has been confirmed only by Siegler and Fein.[4] On the other hand Hartman,[5] working with a large number of monkeys, could induce only infrequent ovulations by mare serum gonadotropin injections (7 per cent of 104 animals). He observed varying degrees of ovarian stimulation in most of his animals, but a considerable number remained refractory. The

1. Westman, A.: Untersuchungen über die Wirkung des gonadotropen Hypophysenvorderlappenhormones, Antex (Leo), auf die Ovarien der Frau, Acta obst. et gynec. Scandinav. **17**: 492, 1937.
2. Moricard, F., and Saulnier, F.: Développement folliculaire provoqué dans l'ovaire de femme au moyen de l'injection de mitosine sérique (hormone gonadotrope du sérum de jument gravide), Bull. Soc. gynéc. et d'obst. **27**: 132 (Feb.) 1938.
3. Davis, M. E., and Koff, A. K.: The Experimental Production of Ovulation in the Human Subject, Am. J. Obst. & Gynec. **36**: 183 (Aug.) 1938.
4. Siegler, S. L., and Fein, M. J.: Studies in Artificial Ovulation with the Hormone of Pregnant Mares' Serum, Am. J. Obst. & Gynec. **38**: 1021 (Dec.) 1939.
5. Hartman, C. G.: The Use of Gonadotropic Hormones in Adult Rhesus Monkey, Bull. Johns Hopkins Hosp. **63**: 351 (Dec.) 1938.

stimulation consisted chiefly of follicular enlargement and only an occasional corpus luteum.

Among the conditions which appeared, on theoretical grounds, to be suited to therapy with this form of gonadotropin were those in which there was a failure of ovulation. Certain cases of amenorrhea, oligomenorrhea and menorrhagia are included in this category. Functional sterility in some patients is also supposed to result from a defective ovulation mechanism. Successful treatment of the latter condition would, of course, be a great boon to these childless couples. Whether or not the ovum from such an artificially induced ovulation would be normal at all times remains to be demonstrated. Other suggested indications are menstrual dysfunctions due to abnormal follicular development and some types of testicular dysfunction, including defective sperm formation.

The reports on the clinical trials with this substance have been, unfortunately, rather unsatisfactory to date. Bowes [6] reported satisfactory results in regulating the menses in four out of five patients. Kennedy and Shelton [7] have likewise reported beneficial responses in three cases of menorrhagia and eleven cases of amenorrhea. The data in these reports were clinical only. The recent report of Hall [8] disclosed extraordinary results in a large group of patients (135). Eight of seventeen patients with genital hypoplasia were reported "cured," twenty-four of forty-three sterile women became pregnant, and 57.6 per cent of those with menstrual disturbances were also "cured." This work requires confirmation, since no other investigators have approached the success of Hall and since no objective evidence was presented by this investigator. Severinghaus and his associates [9] have used gonadotropic hormone from serum of mares in both males and females with encouraging results.

The investigations of Gray [10] are the first to include laboratory data which demonstrate the effect of the mare gonadotropic substance on the reproductive tract of women with menstrual disturbances. This worker at intervals took biopsies of the endometrium of his patients before and after therapy was instituted. In four of eleven cases of secondary amenorrhea the endometrium was changed to the secretory type after two to thirteen months of treatment. Eight of the eleven patients responded with regular menstruation or "fairly so." In seven cases of menorrhagia with endometrial hyperplasia bleeding was unchecked after one to sixteen months of treatment, and there was little effect on the endometrium. In seven cases of metrorrhagia, two responded with regular menstruation. The others were not significantly affected, and only one endometrium was altered to the premenstrual type. In six patients with "minor metrorrhagia" there was improvement in only one.

Gray questioned Hall's results in treating functionally sterile women: "One is led to presume that 55 per cent [twenty-four of forty-three] of cases with sterility, at least in that series, were due to failure of ovulation. In our opinion sterility due to failure of ovulation in a woman with normal, regular menstrual periods is a distinct rarity."

In the male, Kunstadter [11] has reported satisfactory results in cryptorchism and hypogenitalism in boys treated with mare gonadotropin, but there appears to be, from his results, no advantage for this therapy over that with chorionic gonadotropin. Recently Rowlands and Spence [12] have shown that mare serum gonadotropin was rather unsatisfactory in the treatment of cryptorchism. Furthermore, a state of refractoriness was induced when this substance was administered for several weeks, which appeared to be due to the development of an antigonadotropic substance. No competent studies on the treatment of other disorders of the male gonads (including sterility) with mare gonadotropin are available to date.

The evidence in the literature, which forms the basis of this report, except for several lesser references, is definitely inadequate as a basis for the recommendation of therapy with mare gonadotropin. Our knowledge of the physiologic and pathologic action in primates, especially man, is still most uncertain. Certainly there is little justification for claims of consistent therapeutic success in gonadal disorders on the basis of the physiologic reactions obtained in laboratory animals and the meager clinical data reported up to the present time. It is apparent that adequate investigations from the laboratory standpoint, which should include endometrial biopsies, hormonal assays, vaginal smears and chemical studies, are essential for the proper evaluation of the effect of this gonadotropic substance on the abnormal as well as the normal human ovary, and secondarily on the accessory sex organs.

Further experimentation is obviously required under suitable conditions and by investigators whose special training qualifies them for the appropriate study of this material. Until the time when the status of gonadotropin from serum of pregnant mares may be properly evaluated, physicians are cautioned that the use of this substance is still in the early experimental stage, that the claims made by the manufacturers are without satisfactory foundation, and that additional publication of more satisfactory evidence is necessary before this substance should be used in routine practice.

The Council, therefore, voted that the preparations of gonadotropin from serum of pregnant mares marketed as Anteron (Schering Corporation), Gonadogen (the Upjohn Company) and Gonadin (Cutter Laboratories) be declared unacceptable for inclusion in N. N. R., since their advertising claims for its therapeutic use are based on an insufficient amount of scientific evidence and inadequate confirmation of reported results. The right, under the Council's rules, of any firm to the use of a proprietary name for this substance was not considered at this time.

6. Bowes, Kenneth: Treatment of Menstrual Irregularities by a New Sex Hormone Preparation: Preliminary Note, Brit. M. J. **2**: 904 (Nov. 6) 1937.
7. Kennedy, R. B., and Shelton, C. F.: The Mare Serum Hormone in the Treatment of Certain Endocrine Dysfunctions in Women: A Clinical Study, J. Michigan M. Soc. **38**: 209 (March) 1939.
8. Hall, G. J.: Gonadotropic Hormone of Pregnant Mares' Serum: Its Clinical Use in Gynecology, California & West. Med. **51**: 159 (Sept.) 1939.
9. Sevringhaus, Elmer L.: Treatment of Gonadal Hypofunction, Bull. New York Acad. Med. **16**: 53 (Feb.) 1940.
10. Gray, L. A.: Effect of Pregnant Mares' Serum Hormone on the Abnormal Ovary, South. M. J. **33**: 160 (Feb.) 1940.
11. Kunstadter, R. H.: The Treatment of Hypogenitalism in the Male with the Gonadotropic Principle of Pregnant Mares' Serum, Endocrinology **25**: 661 (Nov.) 1939.
12. Rowlands, I. W., and Spence, A. W.: Production of Antigonadotrophic Activity in Man by Injection of Extract of Pregnant Mares' Serum, Brit. M. J. **2**: 947 (Nov. 11) 1939.

NEW AND NONOFFICIAL REMEDIES

THE FOLLOWING ADDITIONAL ARTICLES HAVE BEEN ACCEPTED AS CONFORMING TO THE RULES OF THE COUNCIL ON PHARMACY AND CHEMISTRY OF THE AMERICAN MEDICAL ASSOCIATION FOR ADMISSION TO NEW AND NONOFFICIAL REMEDIES. A COPY OF THE RULES ON WHICH THE COUNCIL BASES ITS ACTION WILL BE SENT ON APPLICATION.

PAUL NICHOLAS LEECH, Secretary.

ALLERGENIC EXTRACTS-MULFORD (See New and Nonofficial Remedies, 1940, p. 32).

The following additional products have been accepted; they are marketed in 5 cc. ampule vials:

Products marketed in dilutions representing 0.005 mg. of nitrogen per cubic centimeter:

Rat Hair.[4]

Products marketed in dilutions representing 0.05 mg. of nitrogen per cubic centimeter:

Allspice,[1] *Aniseed,*[1] *Caraway Seed,*[1] *Cashew Nut,*[1] *Gelatin (Cattle),*[10] *Hazelnut,*[1] *Hops,*[2] *Horse-Radish,*[2] *Mace,*[1] *Pimento,*[2] *Poppy Seed,*[1] *Sage,*[1] *Tapioca,*[1] *Thyme.*[1]

Products marketed in dilutions representing 0.25 mg. of nitrogen per cubic centimeter:

Currant,[2] *Pigeon Feathers,*[4] *Turkey Feathers.*[4]

Products marketed in dilutions representing 0.5 mg. of nitrogen per cubic centimeter:

Anchovy,[3] *Butterfish,*[3] *Castor Bean,*[11] *Catfish,*[3] *Chickory,*[1] *Date,*[2] *Lime,*[2] *Pike,*[3] *Porgy,*[3] *Quince,*[2] *Sardine,*[3] *Weakfish,*[3] *Whitefish.*[3]

Product marketed in a dilution representing 0.75 mg. of nitrogen per cubic centimeter:

Feathers Mixed (Chicken, Duck and Goose).[4]

Castor Bean, marked 11, is prepared for extraction as follows:
The material is ground and washed with toluene and ether until the washings are colorless. The residue is extracted with buffered salt solution for seventy-two hours at room temperature. The extract is boiled for three minutes and filtered through a Mandler candle.

MAGNESIUM TRISILICATE (See THE JOURNAL, April 6, 1940, 1355).

The following dosage form has been accepted:

Tablets Magnesium Trisilicate, 0.324 Gm. (5 Grains).
Prepared by the Smith-Dorsey Co., Lincoln, Neb.

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

535 NORTH DEARBORN STREET - - - CHICAGO, ILL.

Cable Address - - - - "Medic, Chicago"

Subscription price - - - - - Eight dollars per annum in advance

Please send in promptly notice of change of address, giving both old and new; always state whether the change is temporary or permanent. Such notice should mention all journals received from this office. Important information regarding contributions will be found on second advertising page following reading matter.

SATURDAY, DECEMBER 7, 1940

THE PLATFORM OF THE AMERICAN MEDICAL ASSOCIATION

The American Medical Association advocates:

1. The establishment of an agency of the federal government under which shall be coordinated and administered all medical and health functions of the federal government exclusive of those of the Army and Navy.

2. The allotment of such funds as the Congress may make available to any state in actual need, for the prevention of disease, the promotion of health and the care of the sick on proof of such need.

3. The principle that the care of the public health and the provision of medical service to the sick is primarily a local responsibility.

4. The development of a mechanism for meeting the needs of expansion of preventive medical services with local determination of needs and local control of administration.

5. The extension of medical care for the indigent and the medically indigent with local determination of needs and local control of administration.

6. In the extension of medical services to all the people, the utmost utilization of qualified medical and hospital facilities already established.

7. The continued development of the private practice of medicine, subject to such changes as may be necessary to maintain the quality of medical services and to increase their availability.

8. Expansion of public health and medical services consistent with the American system of democracy.

LIFE-SAVING SERVICE WITHOUT RECOGNITION

The disaster to the U. S. S. *Squalus,* the submarine from which a considerable number of lives were salvaged, is no doubt still fresh in the minds of many American citizens. Few people realize, however, the part played by the Medical Corps of the United States Navy in the saving of life in this catastrophe. Early in June 1939 the submarine *Squalus* dived to the bottom and did not come up. Apparently water had rushed into the submarine, and twenty-six men who had been locked in the flooded compartments perished. In the forward compartments were thirty-three men who still lived. Twenty-four hours after the *Squalus* sank the Navy had its experts and rescue devices on the scene. Divers went down in a diving bell, slid a shackle over a ring on the deck of the submarine and attached a cable. Then the rescue bell was clamped over a hatch on the sunken ship, the hatch was opened, and one officer and six seamen climbed into the bell and were raised to the surface. By this process, in a period of eight hours every living man aboard the *Squalus* was taken into the bell. Except for an accident which occurred on the final trip, all were released in that time. One officer and seven men were held in the bell by a jamming of the cable, which, however, was finally cut so that all were rescued.

The saving of the men on the *Squalus* was possible largely because of some extraordinary scientific investigations made by members of the United States Navy Medical Corps in the years since 1932. In those investigations Lieut. Albert R. Behnke contributed notably. A series of papers has been published in the *United States Naval Medical Bulletin.* These investigations, which are concerned with a determination of the cause of accidents with the submarine escape apparatus, the narcotic action of nitrogen, the development of the use of helium, improvements in decompression tables, the development of an effective method of utilizing oxygen in the treatment of air embolism and the discovery that the diffusion of helium through the skin may be used as a measure of peripheral circulation are all fundamental contributions, on which rescue work such as that involved in the saving of the men on the *Squalus* must be based.

Significantly, in all of these investigations, involving more than twenty-five individual contributions to scientific medical literature, the physicians have themselves submitted to various tests before any enlisted men were permitted to volunteer for such a purpose. The value of their work is shown by the fact that only two minor cases of bends developed out of 640 dives, whereas bends occurred almost daily in previous rescue work even though the depths were much less.

The story of the salvaging operations on the U. S. S. *Squalus* was published in the *United States Naval Medical Bulletin* for October 1939. The *Squalus* disaster provided a crucial test for the preparation which Navy medical officers had made over a long period of time. The medical discoveries already mentioned were supplemented by some engineering innovations involving the fabrication of fireproof, electrically heated garments for cold-water diving, improved recirculation of gas through the diver's helmet and the perfection of telephone communication. Indeed, these also were medical as well as engineering problems before they were finally perfected by the engineers. It was found that diving in semidarkness to a depth of 240 feet for the purpose of tunneling under the submarine and attaching the hoses was too dangerous when divers breathed air. The accumulation of carbon dioxide and nitrogen narcosis impaired neuromuscular coordination to such an extent that simple tasks could be carried out only with great difficulty. The substitution of helium for nitrogen in the air minimizes the narcotic symptoms associated with air breathing under pressure. Substitution of oxygen for air or a helium-oxygen mixture in the lungs allows

excess nitrogen or helium gas to diffuse from the body at a maximum pressure head.

The complete story of the *Squalus* disaster and the rescue has not yet, of course, been told. At this time, however, not one of the three medical officers in attendance on the *Squalus,* including Lieuts. Oscar D. Yarbrough, Albert R. Behnke and Thomas L. Willmon, has been given any special award in recognition of his performance. With the exception of two pharmacist's mates, none of the Hospital Corpsmen who worked in this disaster have been recognized by an award. Nevertheless, practically every other officer and Naval "rating" who took part in the salvage has apparently been given special recognition. The reticence of the medical profession in seeking rewards for such service is proverbial. In this instance, when the attention of all the world was focused on the plight of the men who sank in the *Squalus,* when it is recognized that only years of preliminary efforts on the part of medical investigators in the United States Navy made possible the salvaging of those who were saved, when it is recognized that these men in person and the Hospital Corpsmen who were associated with them were in attendance on the actual salvaging operation, neglect to give them the type of special award given to the nonmedical personnel is so evident as to demand this statement. Organizations which know how to impress their opinions on government officials might well adopt official actions to indicate their belief in the justice of the claims of these men to governmental recognition.

SELENIUM AND DIETARY PROTEIN

Within the past few years the etiology of "alkali disease," a condition affecting horses, cattle, swine and poultry of certain areas of South Dakota, Nebraska and Wyoming, has been elucidated.[1] Wheat, corn and barley grown on soils of these areas contain selenium, a chemical cousin of sulfur; this element is definitely associated with the protein fraction of "toxic" grain.[2] A preliminary report recently announced the actual isolation from seleniferous plant material of a crystalline organic compound containing selenium and having the properties of an amino acid.[3] Selenium also occurs in body protein of animals fed for long periods on selenized grains.[4] This selenium behaves in some respects like that found in proteins of selenized grain, and possibly the toxic element is present in a similar chemical combination in both cases.

As persons living in areas where "alkali" disease is endemic also ingest food containing selenium, it seemed possible that chronic selenium poisoning might also be encountered in residents of these areas. Nevertheless, despite the fact that persons in selenium-endemic areas may consume this substance in food up to 0.2 mg. per kilogram of body weight daily, convincing evidence of serious chronic selenium poisoning from this source has never been reported in man.[5] A possible explanation of this situation is afforded by the observation that in animals the toxicity of selenium which is chronically ingested in food is influenced greatly by dietary factors.[6] It has been found, for instance, that an amount of selenium which will cause extensive tissue damage to animals on a diet low in protein and high in carbohydrate will do little or no harm to animals maintained on diets high in protein and low in carbohydrate. Moreover, not only the toxicity of naturally occurring food selenium but also the toxicity of sodium selenite is influenced by the amount of protein in the diet.[6]

Smith [5] has pointed out that the toxicity of selenium in food seems to be determined within certain limits by the ratio of selenium to protein in the diet rather than by the level of selenium in the food as heretofore supposed. This aspect of the selenium problem has been confirmed and extended in a recent report by Gortner,[6] who observed that the quality as well as the quantity of protein in seleniferous diets assumes a role in determining the toxicity of selenium. Casein and lactalbumin tend to counteract the toxicity of selenium, for instance, while edestin and gelatin are not effective in this respect. These recently discovered relationships between the toxicity of selenium in food and the quality and quantity of the protein in the diet have an important bearing on the question of selenium as a health hazard to man and they serve to emphasize once more the fundamental importance of good diets in the maintenance of public health.

1. Selenium Problem, editorial, J. A. M. A. **104:** 50 (Jan. 5) 1935; Toxic Effects of Selenium, ibid. **106:** 926 (March 14) 1936.
2. Horn, M. J.; Nelson, E. M., and Jones, D. B.: Studies on Toxic Wheat Grown on Soils Containing Selenium, Cereal Chem. **13:** 126, 1936.
3. Horn, M. J., and Jones, D. B.: Isolation of a Crystalline Selenium-Containing Organic Compound from Plant Material, J. Am. Chem. Soc. **62:** 234 (Jan.) 1940.
4. Westfall, B. B., and Smith, M. I.: The Distribution of Selenium in Plasma and Liver Proteins and Its Fractionation in Tryptic Liver Digests, Pub. Health Rep. **55:** 1575 (Aug. 30) 1940.
5. Smith, M. I.: The Influence of Diet on the Chronic Toxicity of Selenium, Pub. Health Rep. **54:** 1441 (Aug. 4) 1939.
6. Gortner, R. A., Jr.: Chronic Selenium Poisoning as Influenced by Dietary Protein, J. Nutrition **19:** 105 (Feb. 10) 1940. Smith.[5]

Current Comment

TEACHING OF SOCIAL MEDICINE

According to a recent study "A total of 715 courses covering one or more topics on social medicine was offered by 139 colleges and universities."[1] In addition there were more than a thousand courses in which one or more lectures were devoted to some aspects of social medicine. The 715 full and part courses were analyzed as to the frequency of the topics included. Thus, 432 courses treated "social and economic problems affecting public and individual health," 295 dealt with "health insurance, general," 180 with "voluntary health insurance," and 37 with "compulsory health insurance." There were 112 full courses on social medicine given at sixty-three colleges and universities. These are scattered through a variety of departments, some of which would

1. Hirsh, Joseph, and Pritchard, Elizabeth G.: Teaching of Social Medicine in Liberal Arts Colleges and Universities, Pub. Health Rep. **55:** 2041 (Nov. 8) 1940.

seem to be scarcely related to the subject. Twenty courses are in the department of biologic sciences, thirty-eight in physical education and hygiene, twenty-seven in social work and thirteen in sociology. None of the courses were found in departments of economics and history. Comments would seem to indicate that the courses given in the departments of biologic sciences and physical education and hygiene place the emphasis on treatment of individual and social health rather than on broader questions of policy in the organization of medical services. The fact that 512 full or part courses deal with some phase of health insurance arouses curiosity as to the extent to which such courses are descriptive and analytic and how much of them are propaganda. The fact that little use has been made in any of these courses of the material on these subjects in the Bureau of Medical Economics of the American Medical Association may indicate that most of the information placed before students is derived by prejudiced instructors from private, foundational and governmental propaganda institutions and is largely colored by these sources.

THE POST HAS NEVER SEEN A VITAMIN!

An advertisement for the *Saturday Evening Post*, November 27, was headed "Two Things You Never Saw Photographed." More than half of the advertisement is a reproduction of an f:6.3 Eastman anastigmat lens, with the following text:

In a Dutch prison in Java over thirty years ago, a young medical officer noticed that prisoners eating polished rice were suffering. Then he made the discovery that the trouble was caused not by something *present* in the rice, but by something *absent*—something hidden in its silvery skin. Something we now call a vitamin.

Scientists have traced a dozen evils to missing vitamins—from beriberi to night blindness. They know that some foods are rich in vitamins. And some are not. But you never saw a *picture* of a vitamin, did you?

If the writers of the *Saturday Evening Post* advertisement had consulted the many vitamin research laboratories, both in the industry and in academic circles, they would have seen photographs aplenty of vitamins—not only of thiamine (in the form of thiamine hydrochloride), the lack of which causes beriberi, but pictures of crystals of vitamin A, of nicotinic acid, riboflavin (vitamin B_2), pantothenic acid, ascorbic acid (vitamin C), the crystalline vitamin D compounds and a number of others. They even used for the illustration a 6.3 lens, when amateur photographers would have known better. Perhaps this incident reflects what is wrong with much so-called scientific copy. The writers are more interested in the "idea" than in scientific accuracy. They could have found, by a very small amount of research first, that many vitamins have been isolated in crystalline form; second, that there are many potent substances that have never been seen. There is the "something" that causes a cancer cell to assume malignancy; there are viruses of a number of serious diseases; there is the "something" that makes men go to war; and then finally there is the birth of an idea. These thoughts we present to the agency with no thought of further recompense than the joy of giving; and that cannot be measured either.

NATIONAL PHYSICIANS' COMMITTEE

Many inquiries have been received relative to a mailing which the National Physicians' Committee for the Extension of Medical Service has just sent, we are informed, to every physician in the United States. In this statement of its postelection position, policy and program, attention is called to the statements made by President Franklin D. Roosevelt and Mr. Wendell Willkie on the subject of socialized medicine previous to the election. The committee points out the importance of sustaining public opinion so that the public will come to understand the vital importance of maintaining the delicate and subtle relationship of doctor and patient and will support the independence of the medical profession. At a meeting of its Management Committee, held in Chicago on November 10, the National Physicians' Committee, says the statement, adopted the following resolutions:

Be it recorded that it is the unanimous opinion of the Management Committee of the National Physicians' Committee that under conditions now prevailing there is a greater and more pressing need than at any previous time for such activities as those of the National Physicians Committee.

Be it recorded as the unanimous opinion of the Management Committee that we continue the operations of the National Physicians Committee with increased vigor.

With this decision the National Physicians' Committee has sent to the medical profession a list of activities and objectives proposed for the coming year and a plan for sustaining the organization so that it will be able to function effectively. This statement follows:

NATURE OF ACTIVITIES AND OBJECTIVES

It is essential that funds be provided for:

1. A continuous flow of articles to more than eighty medical journals.

2. Stimulating discussion of this all-important issue in forty-eight state medical meetings, in the meetings of two thousand county medical societies, and hundreds of sectional and special medical meetings and conferences.

3. Preparing and providing for the preparation of articles and releases for thousands of newspapers and hundreds of magazines, and arranging for their publication.

4. Speakers for medical and public meetings and arranging for physicians appearing before local groups and on local radio broadcasts.

5. Radio broadcasts and the preparation of speeches and radio broadcasts to be generally available, and the providing of electrical transcriptions of short speeches and radio broadcasts and arranging for their effective use.

6. The maintaining of strategically important public contacts.

7. The arranging of conferences with boards of hospitals and clinics; business, industrial and other lay groups; and for group meetings of laymen.

all to the end that:

(*a*) political control of medicine can be avoided;

(*b*) the independence of the profession and the pattern of medical practice be preserved; and,

(*c*) the American people can be resold on the incomparable advantages of the American Way of Life.

The medical profession generally has been asked to contribute to a furtherance of these commendable objectives. The work of the National Physicians' Committee, which is wholly in charge of its own Board of Trustees, thus contemplates an expanded program of public enlightenment. Since new legislation in the field of medical service is constantly before Congress, an agency of this type will find a large field for its service.

MEDICAL PREPAREDNESS

In this section of The Journal each week will appear official notices by the Committee on Medical Preparedness of the American Medical Association, announcements by the Surgeon Generals of the Army, Navy and Public Health Service, and other governmental agencies dealing with medical preparedness, and such other information and announcements as will be useful to the medical profession.

THE 1940-1941 MILITARY TRAINING PROGRAM

Participation of the Medical Department of the Army

Uppermost in the minds of all physicians at present is undoubtedly the question of national defense. The medical departments of the armed forces must plan to meet the immediate twofold problem of furnishing an adequate medical service to the men of our unprecedented peacetime Army and Navy, and of training the large number of Medical Department trainees who, at the expiration of their twelve months military service, will pass to the Enlisted Reserve Corps. They will furnish the trained personnel required for mobilization in the event of a national emergency. The Surgeon General of the Army has furnished the following outline regarding the participation of the Medical Department of the Army in the 1940-1941 military training program:

THE NEED FOR PERSONNEL

The total strength of the army of the United States next spring will be approximately 1,400,000. This represents a Regular Army of 400,000 officers and men, the National Guard of the several states federalized as the National Guard of the United States, numbering 200, 000, and citizens selected for military training during the coming twelve months—about 800,000 in number. The latter will receive their training in active units of the Regular Army and of the National Guard, in Regular Army inactive units activated for training purposes, in the numerous installations required for the overhead of these forces and in enlisted replacement centers throughout the nine corps areas of the country.

PROVISION OF HOSPITAL BEDS

The Medical Department is charged with providing adequate medical service for the entire army of the United States at posts, camps and stations within and beyond the continental limits of the United States. In each military station in the United States there will be a hospital with four beds for each hundred of the military population. The operating room, kitchen, messing facilities and clinics in each of these hospitals will be of sufficient size to provide service for an additional patient per hundred men so that in an emergency it will be necessary to construct only the additional ward buildings. Furthermore, there will be general hospitals suitably located throughout the United States to provide an additional bed per hundred of the military population.

The provision of 5 per cent of hospital beds which can be rapidly expanded to 6 per cent may appear excessive when compared with hospitalization provided for the civilian population of this country. However, all of the military sick, including such cases as in civilian life are ordinarily cared for in their homes, must be treated in hospitals, since they cannot receive satisfactory care in the barracks. In addition, when young adults are brought together in large groups, contagious and infectious diseases that spread rapidly under such conditions occur much more frequently than in civil life. Furthermore, sufficient beds must be provided for the care of the sick during the winter and spring seasons of the year, when there is always an excessive number of such cases.

Scattered throughout the large camps or stations there will be dispensary buildings and dental clinics for the infirmary care and dental treatment of the personnel. In addition, in each large camp there will be a medical headquarters, with properly qualified scientists for the general supervision of the medical activities, including the protection of the health of the troops, the careful inspection of food products and the general supervision of the nutrition of the men.

The Medical Department will be charged with the training of the medical detachments and the medical department units of the Regular Army and the National Guard, and with the instruction of the service personnel in hospitals and other installations. It is also responsible for the preparation of the trainees in enlisted replacement centers, in hospitals and in service schools, who will receive there the individual Medical Department instruction which will permit their incorporation in organizations for further unit training.

REQUIREMENT OF PHYSICIANS

The initial requirement will be approximately 6.5 doctors for each thousand men in the military service. Rapid calculation will show that the total number for an army of 1,400,000 men will be 9,100 doctors. Additional ones may be required, but in the interest of economy the initial procurement will be limited to the number stated. The 1,200 physicians in the Regular Army and the 1,100 in the National Guard are included in the total, leaving approximately 6,800 physicians to be supplied by the Reserve Corps. There are now in active service or under orders approximately 1,500 Reserve physicians, leaving 5,300 to be procured during the next few months.

STATUS OF THE RESERVE CORPS

Under the recent joint resolution passed by the Seventy-Sixth Congress, the President is authorized to order into the active military service of the United States for a period of twelve consecutive months each any or all members of any Reserve component of the Army of the United States, with or without their consent, to such extent and in such manner as he may deem necessary for the strengthening of the national defense. If a sufficient number of officers do not indicate their availability for this service, Reserve officers must necessarily be ordered to duty without their consent. Additional appointments among physicians of draft age will increase the strength of the Medical Corps Reserve. However, it is apparent that a large percentage of these officers must participate actively in the present program for preparing a portion of the country's man power for national defense.

In establishing rosters from which officers will be ordered to duty, corps area commanders and chiefs of

branches have been instructed to circularize all Reserve officers under their assignment jurisdiction to permit them to state the amount of deferment desired and the cogent, pertinent reasons for such deferment in the event that they are not immediately available for military service. This action has been taken in view of the fact that a national emergency has not been declared by the Congress, nor has mobilization been ordered. The medical service of a training program, although essential to national preparedness, possesses none of the glamour of the same service during actual military operations; it is, however, equally important. Indeed, military training may, through the thoroughness of its preparation for war, materially assist in preventing the necessity of participation in military operations. It is realized, of course, that all officers would express their immediate availability in the event of war; many, however, feel that their services are not of national importance at the present time.

Both the economic and the rational utilization of medical officers is essential. It is planned that as far as possible qualified officers will be selected for assignment to duty with units and at installations according to their previous training and experience. Accordingly, selection must be qualitative as well as quantitative in order that the specific requirements of a modern medical service may be properly met. Officers selected for duty will be given the maximum possible advance notice of such action.

INFORMATION FOR MEDICAL RESERVE OFFICERS ORDERED TO DUTY

In this connection the Surgeon General has suggested that the following points be brought to the attention of all Reserve medical officers:

1. When notified that you have been selected for active duty, submit at once the required report of physical examination. The disclosure of disqualifying defects prior to the issuance of orders may prevent a disruption of your practice or civil employment.

2. Orders issued will place you on active duty at your home or, if a temporary change of address has been submitted, at that location, and will direct you to report to a specific post, camp or station for duty.

3. Travel to your station may be accomplished by automobile, but no delay will be granted for that purpose above the customary time for travel by rail.

4. You will be reimbursed for travel at the rate of 8 cents a mile, based on the shortest usual railway route to your station.

5. Transportation for dependents to your first station will not be furnished by the government. It is perhaps advisable that your family not accompany you, since the housing problem at or within the vicinity of Army stations is frequently acute.

6. If you have no uniform and military equipment, these may be purchased at your first station.

7. Pay and allowances are as shown in the accompanying table.

Pay and Allowances of Medical Reserve Officers

Grade	Annual Base Pay	Allowances: Rental Allowance, With Dependents	Allowances: Rental Allowance, Without Dependents	Allowances: Subsistence Allowance (30 Days), With Dependents	Allowances: Subsistence Allowance (30 Days), Without Dependents
Colonel	$4,000	$120	$80	$36	$18
Lieutenant Colonel	3,500	120	80	54	18
Major	3,000	100	60	54	18
Captain	2,400	80	60	36	18
First Lieutenant	2,000	60	40	36	18

The annual base pay is increased at the rate of 5 per cent thereof for each three years of service up to thirty years. Full time will be computed for all periods during which men have held commissions as officers in the Army, Navy, Marine Corps, Coast Guard, Coast and Geodetic Survey and Public Health Service, or in the National Guard or Naval Militia, the National Naval Volunteers or the Naval Reserve Force or Marine Corps Reserve, when confirmed in grade and qualified for all general service, and with full time for all periods during which they have performed active duty under Reserve commissions, and with one-half time for all other periods during which they have held Reserve commissions.

PHYSICIANS UNDER SELECTIVE SERVICE

Physicians as a group will not be exempt from conscription for military training and service. Their deferment because of importance to civil communities is a function of the local draft boards. Accordingly, it is difficult to approximate the number which will be inducted into the Army. Obviously, the training received by such draftees will be more appropriate and the services rendered the Army of greater value if the physicians who are eligible and qualified for appointment in the Medical Corps Reserve be commissioned in the Officers Reserve Corps for duty as medical officers, rather than continue their training as enlisted men.

Physically qualified graduates of approved schools of medicine who desire appointment in the Medical Corps Reserve for immediate active duty should make application to the commanding general of the corps area in which they reside. Such applications may be submitted either before or after selection for military training and service or after induction into the Army of the United States. No change in the classification of such applicants will, however, be made by local selective service boards until the actual letter of appointment has been received.

APPOINTMENTS IN THE MEDICAL CORPS

Appointments in the Medical Corps of the Regular Army will, in all probability, continue as at present through competitive examinations of Reserve officers who have not passed the age of 32 years at the time of appointment.

WORK OF THE AMERICAN MEDICAL ASSOCIATION

The Surgeon General of the Army, through Lieut. Col. George C. Dunham, the representative of the Medical Department in the House of Delegates, submitted a request to that body at its last meeting in New York, in June 1940, requesting the assistance of the American Medical Association in the classification and procurement of physicians for the Army. It was hoped in this way to procure the physicians required without disturbing too seriously the civilian medical service and at the same time to place the physicians enrolled in positions for which their previous training qualified them. The House of Delegates approved the request of General Magee and appointed a Medical Preparedness Committee. The U. S. Navy and the U. S. Public Health Service made similar requests.

Reference has been made to the action of the House of Delegates and to the working of the Preparedness Committee in previous issues of THE JOURNAL. The Preparedness Committee, the executive officers of the American Medical Association and the chairman and

members of the various state and local committees have all given generously of their time and funds in this work. They have been of material assistance to the Surgeon General and corps area surgeons in the classification and procurement of Reserve Corps medical officers. They generously have offered their assistance in similarly classifying and procuring such physicians as may be required in addition to those in the Reserve Corps. Although the majority of appointments of additional Reserve officers for active duty at this time will be 35 years of age or under, a limited number of properly qualified physicians above this age will be required as chiefs of services of the many large hospitals to be established.

COOPERATION OF MEDICAL PROFESSION

The history of our country has repeatedly shown that there is no more patriotic group than the American physicians. They have always responded generously to their country's call for assistance. At this time, although this country is not engaged in war, the national preparedness program requires an adequate medical service. Without it, the program will be hampered materially. In addition to the adequate care of the sick and protection of the health of our young men in the camps, the Medical Department must be able to train its personnel to act in conjunction with the troops of the other arms and services so that in time of battle, if unfortunately that time should come, it may be able to collect efficiently and evacuate promptly casualties that occur on the battlefield so that each one may receive as promptly as possible efficient medical care. Let us repeat: The success of the national preparedness program depends to a large extent on adequate medical service. American medicine appreciates its obligations and will furnish a sufficient number of properly qualified physicians.

CONFERENCE ON MEDICAL PREPAREDNESS HELD AT AMERICAN MEDICAL ASSOCIATION HEADQUARTERS, SATURDAY, NOV. 23, 1940

The following were in attendance:

Dr. Irvin Abell, chairman, presiding.
Dr. James A. Crabtree.
Dr. Charles A. Dukes.
Lieut. Col. George C. Dunham.
Dr. Morris Fishbein.
Dr. Roy W. Fouts.
Lieut. Col. C. G. Hutter.
Dr. R. G. Leland.
Brig. Gen. A. G. Love.
Dr. John H. O'Shea.
Dr. Stanley H. Osborn.
Dr. James E. Paullin.
Dr. Walter G. Phippen.
Lieut. Col. C. B. Spruit.
Dr. Harvey B. Stone.
Dr. Nathan B. Van Etten.
Dr. Olin West.

FORENOON SESSION

Communications were read from Dr. Frederick Rankin of Kentucky and Dr. Samuel E. Thompson of Texas, who were unable to be present.

Remarks on Progress by Corps Area Representatives

Dr. Paullin said that the problem at present in the Fourth Corps Area concerned the distribution of physicians in counties where there were few doctors. They are preparing in those counties for medical care. Problems have arisen in North Carolina, South Carolina and Georgia concerning medical reserve corps officers who have been called into service with the possibility that their communities will lack sufficient medical service. An attempt has been made to settle the problem in each state and Dr. Paullin stated that Georgia has settled it. The second problem in the Fourth Corps Area is that of residents in teaching hospitals where some have been ordered to active duty; the suggestion has been made that they can operate as well with a slightly diminished personnel if those who remain will do a little more work. Through the state and local chairman, all members of the profession are being listed as to whether they can be spared from their communities and the lists are to be given to the corps area surgeons. The medical preparedness organizations have not as yet been functioning well in North Carolina and South Carolina.

Dr. Osborn and Dr. Phippen said that in the First Corps Area they have given the selective service and the local recruiting office all the assistance they have asked for in the way of induction and draft board physicians. A problem that confronts them in Massachusetts in completing the survey questionnaire is that of 2,400 nonmembers of the Massachusetts Medical Society, including a lot of men from nonaccredited medical schools. Dr. Abell asked whether these men from nonaccredited schools would be eligible for commissions, and Brig. Gen. Love stated that they are not eligible now.

Dr. Dukes said that in the Ninth Corps Area questionnaires have been slow coming in because of the great distances involved; also some of the younger men hesitate to sign, fearing it will put them under obligations that they do not want to assume at present. The distances involved have made a difficult problem of supplying physicians for the boards also, although the necessary number has been provided. This difficulty does not affect California as much because of the larger number of physicians available. Dr. O'Shea said that members of the Washington State Medical Society had answered the questionnaire 100 per cent and that the entire state had returned now, 93 per cent. The problem of induction boards in the northern part of the Ninth Corps Area has been difficult. The board at Missoula, Mont., had to be drawn from the breadth of the entire state. The same situation existed at Boise, Ida., where there were not sufficient specialists for the induction board. At Vancouver it was necessary to get some specialists from Portland, Aberdeen and Noquiam.

Dr. Stone reported that the induction boards had been completed in the whole Third Corps Area. With regard to the survey questionnaire, there has been much difficulty in this area in physicians not receiving the questionnaire. Great interest has been shown by hospitals and medical schools about possible disruption of their staffs by the drafting of house men. Assurance has been given that the draft officers will use discrimination so that no institution will be badly disorganized by inductions from its staff. The availability of some physicians in some communities in the Third Corps Area, as well as some health officers, came up. Dr. Osborn pointed out that the state health officers in conference with the three surgeon generals agreed that the state health officers would forward to the U. S. Public Health Service, which would forward to the surgeon generals of the army and navy, a list of health officers who it was felt were indispensable to maintain civilian health. Each state health officer has

already sent a list of indispensable employees to the U. S. Public Health Service. These lists were sent to the surgeon general of the army, who has sent copies of them to the corps area surgeons. General Love said that some of these lists apparently had been turned over to subordinates, who included in the list not only the key man but all of the men, even nurses and technicians.

Dr. Fouts of the Fourth Corps Area reported that 83.8 per cent of the survey questionnaires had been returned. Nebraska had returned 97 per cent. He supplied a list of men for the draft boards to the Adjutant General of the National Guard, Nebraska, which was submitted to the governor. Thus far he has made no recommendations for appointments on the medical advisory boards in Nebraska. He has furnished the corps area surgeon with adequate lists of specialists for service on the induction boards and at the next call in January each board will make its own arrangements with men on this list who have agreed to the call, understanding that they would not serve several days in succession but a day at a time, if possible. Dr. Fouts said that he could not provide four neuropsychiatrists for the induction boards if it requires a week or ten days of their time to go great distances away from home. There are not four neuropsychiatrists, he said, in the state of North Dakota, and how he is to get four for the board at Fort Crook is a question. An adequate panel has been turned over to the corps area surgeon for the induction boards on whom his induction board administration can call.

Colonel Spruit pointed out that it does not require four men for a board but one psychiatrist at the rate of every fifty inductants examined.

Dr. Fishbein said that in the sparsely settled states one psychiatrist would be able to give the psychiatric examinations. Circular No. 1 defined the examination simply as sufficient to rule out insanity but not the kind of examination that the average psychiatrist thinks of making when he makes an examination for legal purposes.

Dr. West said that apparently this problem in New York had been well attended to and the demands of the corps area satisfied. In New Jersey the committee has been active, but they have had some difficulties having to do with the selection of examiners for local draft boards and for advisory boards. Some governors of states have called on state committees for a list of names for consideration for appointment as medical examiners and then have paid no attention to the recommendations submitted to them but in one or two instances have put on osteopaths. Dr. Fouts said it was true in Nebraska, where they had to work over the list the third time. Colonel Spruit asked to be informed concerning unqualified men who might be appointed as examiners. Dr. West said that the request was transmitted to every state chairman and members of the Committee on Medical Preparedness. Colonel Spruit should receive all the information available about unqualified men that have been nominated to serve in these capacities by governors of states, as he is anxious to keep such men off the boards as far as it is possible to do so.

Colonel Spruit said that incompetent physicians will show up in the results of their physical examinations, as he has had occasion to observe in the first reports of examinations from some states. One man was passed who was 6 feet tall and weighed 138 pounds, and another accepted for the draft had a perforated ear drum, both causes of rejection. Incompetent physicians on these boards can be removed if the traveling inspectors believe they are not doing a good job. The examining physicians and appeal boards are under national control, and it may be that the medical advisory boards will be placed under national control.

Dr. West said that a few men had already been commissioned in the reserves and assigned to active duty for whom the A. M. A. headquarters had no record whatever. The War Department had not asked these headquarters to check over the lists before these men had been commissioned or assigned to duty. General Love stated that they would be very glad to have a list of these names and to investigate them.

The committee asked that official lists of all physicians in selective service, and on local examining boards and medical advisory boards, and the legal member on the appeal boards be sent to the American Medical Association headquarters for checking by the Bureau of Investigation.

AFTERNOON SESSION

Report on Survey of Committee on Medical Preparedness

Dr. Leland reported on the survey being conducted by the Committee on Medical Preparedness. Since July 5, 126,489 schedules have been received. Of that number 81,853 have had the information transferred to punch cards. Of those 50,000 have been sorted in various ways for the listing of specialists, of general practitioners and of physicians in special classifications. The specialists have been listed by states for about 50,000 punch cards. Eighteen thousand general practitioners are now being listed on a specially devised form. The specialty lists are being sent to special committees that will provide the Committee on Medical Preparedness with additional information concerning residencies completed, recognized postgraduate work that the specialist has taken, and the qualifications of specialists as administrators and as teachers and research workers. Shortly, many more of these cards will be run and more names compiled on these listing sheets, giving information on additional numbers of physicians. Lists were received from some state chairmen of physicians for the Induction Boards in their areas and these were accepted at face value. Faculties of medical schools have provided the Committee with lists of teachers considered essential to the operation of the school. Many state chairmen have given much time to stimulating physicians to return their schedules. Some states have reached almost 100 per cent and others are still working diligently. Later, if a schedule from a physician over 70 years of age is not received, one will be filled out in the headquarters with the information contained in the American Medical Directory and placed in the files. Some of these men would be suitable for civilian medical care. Generally, the work in connection with the census is proceeding satisfactorily.

Questionnaires on Industrial Medicine

A special questionnaire was sent to all physicians who indicated that they were interested in devoting themselves to industrial practice. Dr. Leland thought that, when this particular survey is completed, about 6,000 industrial practicing physicians will be found.

This census will ultimately provide vast amounts of accurate and complete information which ought to be

put to some use. These headquarters are ready at all times to make the information available to those who need it.

Dr. Abell asked how many of the 126,000 replies received are from men within the active age limit. That information has not been attained yet. Dr. Fishbein, however, stated that he had figured this out for another purpose and found that there were approximately 14,000 physicians in the United States over 60 years of age. Dr. Leland stated that few of the older men refused to volunteer but that a large number of younger men will not or are undecided unless it comes to a matter of immediate war, when they would volunteer at once.

General Love stated that the work done by the various committee men will be a great help to solve the problem of supplying physicians. The idea is for them to have a year of service and then go back and have some one else take their place, unless we get into actual war and unless the physician requests an extension of service.

Dr. Crabtree said that the U. S. Public Health Service would like to have access to these data in case it needs to increase its personnel, as there may be occasion to employ other types of specialists, particularly in tuberculosis and venereal disease and possibly industrial medicine. As yet, Dr. Leland stated, lists on public health specialists or tuberculosis have not been drawn.

The committee voted to accept Dr. Leland's report and adopt it as the official record of the Committee on Medical Preparedness so far in this work.

Fee Schedule for Laboratory and Roentgen Examinations

A subcommittee of the Committee on Medical Preparedness composed of Dr. West, Dr. Fishbein and Dr. Leland previously was appointed to prepare a fee schedule for laboratory and roentgen examinations. The subcommittee obtained a schedule that had been prepared for the state of New York and sent copies to each member of the Committee on Medical Preparedness, each state chairman and the secretary of each state medical association. The committee did not approve this schedule unanimously by mail vote. The selective service system decided that it might be better to have a fee schedule for each state and instructed the state headquarters of the selective service system to confer with the medical societies about formulating schedules and that action relieved the subcommittee of the Committee on Medical Preparedness of responsibility of preparing a fee schedule to be applicable throughout the country.

Dr. West said that those schedules have been returned to him by individual men in various states with notations that some fees on the New York schedule are too high. Dr. Van Etten said that they are a little less than half of the fees provided in the workmen's compensation law in New York and that the laboratory men there were willing to make this concession as a patriotic contribution.

It was moved and voted that the schedules for laboratory and examination fees be left to the individual states and that the subcommittee of the Committee on Medical Preparedness appointed to prepare a fee schedule be discharged.

Corps Area Surgeons to Confer with Members of Committee or with State Chairman

After a discussion by various members present, it was voted that each state committeeman be responsible more or less for the affairs of his state committee through the corps area chairman of the Medical Preparedness Committee and that both of them in cooperation work with the corps area surgeon to accomplish the desired ends or purposes of this committee and that all such information be communicated from one to the other.

Rejection of Registrants with Venereal Disease

General Love said that when the Committee on Medical Preparedness met, September 20, the arrangement at that time was for Wassermann tests to be taken of the registrants at the time of the induction and that all registrants with evidence of venereal lesions would be placed in a limited service class. The Surgeon General's Office considered this matter and decided that it would be better to have the blood specimens taken by the local draft boards, and since this is primarily a military training project, the army would not be warranted in taking in positive cases; that is the explanation of the reversal of policy in this matter as far as the War Department is concerned.

Colonel Spruit pointed out the advantages of having the blood specimens taken by the local boards rather than at the induction centers. Dr. Crabtree said that this procedure will provide a Wassermann dragnet that will find a great amount of syphilis and, if we take advantage of it by placing the positive cases under treatment, will advance syphilis control many years.

Dr. Fishbein said that if we could get, say by January, some statistics on the number of positive Wassermann tests in the first group and on the difficulties involved in applying serologic tests to the first group examined, it would indicate how to do it better when the large group comes along later. It may be necessary to modify some of the procedures fairly soon, and the sooner we learn what is to make these modifications necessary, the quicker the machinery can be set in motion to make the modifications. It is conceivable that by some other sudden order the whole venereal disease situation might be changed again.

It was voted that the remarks of General Love and Colonel Spruit covering this subject be made a part of the record of the Committee on Medical Preparedness.

Communities Deprived of Medical Service

Dr. Abell said that in a few locations in Kentucky and Tennessee some of the younger physicians in the Medical Reserve Corps have been ordered to active duty, leaving certain communities and hospitals deprived of men essential to carry on adequate medical service. The question of selecting men to be ordered to active duty without depriving communities of essential men was fully discussed. It was found that, as General Love stated, there had been a misunderstanding. Dr. West and Dr. Paullin pointed out that the purpose of the Committee on Medical Preparedness was to render definite help to the War Department in the selection of officers and to see that the civil communities were left with sufficient physicians to provide them with medical care. General Love stated that the corps area commanders had been directed to make a survey of reserve officers to determine those who volunteered for active service and those who could be spared from their communities, but that it was difficult for a corps area surgeon to know the requirements of the various communities in his area and to determine what men should be ordered to duty, especially if they volunteer. General Love said that we are trying to get physicians without disturbing practice in the hospitals and schools but that we have to work fast, as within the next three months about 20,000 additional hospital beds will be

opened and physicians must be had to man these military hospitals. We shall need then about 6,000 or 7,000. Dr. Fishbein stated that, if we could go before the profession with definite information about the number needed and the kind of work they need, they will be commissioned first lieutenants and paid so much, and that if their assignment to a hospital will count toward certification for an examining board it would probably be less difficult to get 5,000 physicians to volunteer. [This material appears in the current issue of THE JOURNAL.]

Dr. O'Shea asked whether reserve officers can still resign and General Love said that any one below the grade of captain might resign.

The motion made by Dr. Paullin that the Committee on Medical Preparedness go on record as furnishing to the Surgeon Generals of the Army, Navy and the Public Health Service a statement that the committee is willing to cooperate with them fully whether for preparedness or for war, after full discussion, was adopted.

Dr. Paullin also moved that each state committee chairman in consultation with the corps area surgeon study the members of the medical reserve corps in the various areas and, in cooperation with local or district committees, determine whether or not their services are indispensable for the community. This was discussed and adopted by the committee.

Graduates of Unapproved and Foreign Schools

Dr. Van Etten read a resolution from Kings County Medical Society, Brooklyn, which brought forth a discussion of whether men from foreign medical schools and from unapproved schools in this country should be commissioned. After discussion by various members, Dr. Fishbein pointed out that the Association, to be consistent, must support the standards of the Council on Medical Education and Hospitals, and that the Committee on Medical Preparedness could therefore only recommend that physicians who are graduates of acceptable American and Canadian schools be considered in selection for commissions. The motion was seconded and carried.

The National Youth Administration

Dr. Crabtree said that the Public Health Service had assigned to each corps area a liaison commissioned officer to expedite relations between the War Department and the public health interest of the communities; they will report for duty December 1 and in any way in which they can be of service to the Committee on Medical Preparedness or the state or local communities, they are available. The Public Health Service is already meeting the usual problems of prostitution, general health and sanitation services, medical service and hospital service in communities adjacent to army camps and industrial developments. These problems have stepped up tremendously in some of these areas, and the Public Health Service needs help.

Dr. Crabtree said that the National Youth Administration has changed its program and now is emphasizing training youth in vocations in essential defense industries. The National Youth Administration asked the Public Health Service to develop a health program for these boys under training, and a medical officer was assigned to see what could be done. In the next year it is estimated that 500,000 youths between 18 and 25 will pass under this supervision and that 60 per cent of them are indigent. This program falls into two categories: (1) a resident project, (2) a nonresident project. In the former the youth is taken from home to some center and put in a dormitory and given vocational training and from $6 to $8 a month. Of these there will be some 100,000. The other 400,000 will live at home but work or go to school locally. The health program as proposed includes a physical examination and an attempt to rehabilitate the boy as far as practicable. In the resident centers they propose to employ a nurse and local physicians.

Dr. Fishbein said that the National Youth Administration is apparently attempting to carry out a medical program without telling the medical profession what it is doing. It should draw up a statement of what it is attempting. He did not think the medical profession objected to helping to take care of these boys. If the National Youth Administration would get to the profession word of what is needed, it will probably get all the cooperation it desires.

Protection of Interests of Physicians Called Into Service

Dr. West said that some communities are working on plans for looking after the interests of doctors called into active service. Dr. Dukes moved that the Committee on Medical Preparedness approve of the activities in certain states with regard to the protection of men who go to service and to approve also of what has been done to protect them legally and that the committee further study this problem and give all assistance possible to men called into service. The motion was seconded and approved.

Status of Interns and Medical Students

Dr. Abell read a letter from the Greater New York Hospital Association addressed to Col. Arthur McDermott, indicating that they had already agreed that the interns and residents in New York hospitals will, under his control, be deferred; that, he said, is what can be done in each state if one wants to by taking it up with the Selective Service headquarters in the state. Dr. Phippen said that this procedure was considered in Massachusetts, where they decided that it would be better to take each individual intern as he came up before his draft board. The Massachusetts Medical Society and the Massachusetts Hospital Association appointed a joint committee to consider such matters. Dr. West brought out that the Surgeon General had said that interns who wish to apply for commissions in the Medical Reserve Corps will be accepted if they can qualify but that they will not be assigned to active duty until they have completed their one year of internship.

Dr. Fishbein moved that the Committee on Medical Preparedness urge on all interns and residents the desirability of a year of service and that a statement be requested from the Surgeon General outlining the circumstances under which interns will be granted reserve commissions. General Love replied that such a recommendation has already been approved in the Surgeon General's Office and is now on the desk of the Chief of Staff of the Army. Furthermore, if an intern is drafted he is still eligible for a commission in the Army, but the Army ordinarily would not call him out until after he had completed his one year's internship. However, that regulation can be changed at any time. Further discussion brought out that the Navy will commission a doctor the day after graduation and give him an internship in a navy hospital. Dr. Abell said

that a number of the specialty boards appear favorable, although no definite action has been taken, to granting recognition for the year spent in that service as applied to their training. Dr. Stone said that the American Board of Surgery had agreed to that in principle with the reservation that if a man desires his service in the Army to apply to certification it would have to be of a surgical nature and not a year of general service in the Army.

Collection of Blood For Transfusion Purposes

After discussion it was moved and voted that the collection of blood for transfusion purposes be referred to a committee of the National Research Council.

Staff Personnel for New Army Hospitals

General Love said that there are to be about 70,000 hospital beds, including those now in use, and one fifth of these will be in general hospitals and the other four fifths in camp hospitals on a 4 per cent basis in each camp and varying in size from 500 beds to 2,000 beds. Between fifty and sixty doctors per thousand beds will be required. With the 20,000 beds already available in army hospitals, about 50,000 additional beds will be provided for. The present age limit for physicians to man these army hospitals is 55 years; there is a possibility that this service may not be limited to one year but may extend to several years.

Dr. Dukes moved that the Committee on Medical Preparedness study this problem and be prepared to nominate from the various districts such men as might be required beyond draft age for the specialty groups that may be called on for the government. The motion was put to a vote and carried.

Letters

Letters were read to the committee from the Dental Preparedness Committee of the American Dental Association, from the National Medical Association and from the secretary of the New York State Medical Association, all of which were discussed. A letter was read also concerning roentgen examination of the chest of drafted men and a badge for physicians serving as examiners but not holding commissions. Dr. O'Shea moved that the subject of the badge be referred to the Executive Committee of the Committee on Medical Preparedness to report back at the next meeting. The motion was carried.

ARMY RESERVE OFFICERS ORDERED TO ACTIVE DUTY

WAR DEPARTMENT

Following is a list of additional medical reserve corps officers who up to November 25 had been ordered to extended active duty with the regular army by direction of the War Department, Washington, D. C.:

APPLEBAUM, Henry, 1st Lieut., New York.
ARMSTRONG, James Harris, 1st Lieut., Oxford, Miss.
BAGNALL, William Stanley, 1st Lieut., San Francisco.
BLOOM, Rudolph, Colonel, Philadelphia.
BOOTH, Edgar Waldo, 1st Lieut., Shreveport, La.
BROWN, Thomas Paul, 1st Lieut., Drexel Hill, Pa.
BURNSTINE, Marcus David, 1st Lieut., Columbus, Ohio.
CASEY, David Timothy, 1st Lieut., Cambridge, Mass.
CHAIN, William Thomas, 1st Lieut., Narberth, Pa.
DENHAM, Robert Hilliard, Jr., 1st Lieut., Grand Rapids, Mich.
ENGELHARDT, David Meyer, 1st Lieut., Warren, Wyo.
FANTUS, Robert Alan, 1st Lieut., Chicago.
FEIMAN, Lawrence Holt, 1st Lieut., Milwaukee.
GARDNER, Leon Philip, 1st Lieut., Aurora, Ill.
GOERINGER, Claire Ferdinand, 1st Lieut., Wilkes-Barre, Pa.
GOLD, Jacob Louis, Captain, New York.
GOLDSTEIN, Isadore Irwin, 1st Lieut., Chicago.
GRINDLAY, John Happer, 1st Lieut., Rochester, Minn.
HAINES, John Wister, 1st Lieut., Philadelphia.
HALL, Robert Milton, 1st Lieut., Denver.
JONES, Warren Candler, 1st Lieut., Sunflower, Miss.
KELLY, Delbert Cleo, 1st Lieut., Hazel Dell, Ill.
KETCHUM, Clarence Wood, 1st Lieut., Atlanta, Ga.
KOLCZUN, Michael Cornelius, 1st Lieut., New Orleans.
LARCHEZ, Albert Robert, 1st Lieut., Arlington, Mass.
LIPSON, Herbert Jacob, 1st Lieut., Grafton, N. D.
MARSHALL, James Moore, 1st Lieut., Conway, S. C.
MATHIS, Earl Nadeau, 1st Lieut., San Francisco.
McCARTHY, Alphonsus Melvin, Major, Electric Mills, Miss.
POWER, William Redmond, 1st Lieut., Merrick, L. I., N. Y.
PRIEST, Allan Eugene, 1st Lieut., Pullman, Wash.
REICHARD-ESTEVES, William, 1st Lieut., Des Moines, Iowa.
RIZZOLO, John, 1st Lieut., Newark, N. J.
SASEEN, Charles Allen, 1st Lieut., Atlantic City, N. J.
SCHOFIELD, John Thomas, Jr., 1st Lieut., Philadelphia.
SVETICH, Edward Michael, 1st Lieut., Joliet, Ill.
TALBOT, John Ralph, 1st Lieut., Marshfield, Wis.
VAN ARSDALL, Condit Brewer, Jr., 1st Lieut., Harrodsburg, Ky.

NINTH CORPS AREA

The following medical reserve officers were ordered to extended active duty by Ninth Corps Area Order for the week ended November 23. The Ninth Corps Area comprises the states of Washington, Montana, Wyoming, Oregon, Nevada, Utah, California and Idaho:

ALTOSE, Alexander R., 1st Lieut., Seattle, Fort Lewis, Wash.
BOLSTAD, Donald S., 1st Lieut., The Dalles, Ore., Fort Lewis, Wash.
COGGIN, Charles B., Captain, Los Angeles, Presidio of Monterey, Calif.
CUSTER, Clarence P., Captain, Patterson, Calif., Presidio of Monterey, Calif.
DARRAH, John R., Captain, Cody, Wyo., Fort Lewis, Wash.
GARDENIER, William H., 1st Lieut., Los Angeles, Presidio of Monterey, Calif.
HARRISON, Alexander V., 1st Lieut., Los Angeles, Fort Lewis, Wash.
KESSLER, Raymond L., Captain, Pendleton, Ore., Fort Lewis, Wash.
MINNA, John B., Major, San Diego, Calif., Presidio of Monterey, Calif.
PRESENT, Arthur J., 1st Lieut., La Jolla, Calif., Presidio of Monterey, Calif.
SCHWARTZ, Irving, Jr., Captain, San Francisco, Presidio of Monterey, Calif.
SHORT, Faulkner A., 1st Lieut., Portland, Ore., Fort Worden, Wash.
WILEY, James W., 1st Lieut., Portland, Ore., Fort Worden, Wash.

NAVAL RESERVE OFFICERS ORDERED TO ACTIVE DUTY

The following medical officers of the U. S. Naval Reserve are under orders for active duty, in addition to the names of those published in THE JOURNAL, November 16. Their rank, home address and station are indicated:

CASON, William M., Lieut. Comdr., Sandersville, Ga., Naval Air Station, Jacksonville, Fla.
CONSTANS, George M., Lieut. Comdr., Bismarck, N. D., State Director of Selective Service, North Dakota.
CRISPELL, Raymond S., Lieut. Comdr., Durham, N. C., Norfolk Naval Hospital, Portsmouth, Va.
DEYTON, John W., Lieut., Asheville, N. C., Naval Air Station, Pensacola, Fla.
GILLEN, James H., Jr., Lieut., Arlington, Va., Nav. Med. Sch., Nav. Med. Center, Washington, D. C., for instruction.
JAMESON, Edwin M., Lieut. Comdr., Saranac Lake, N. Y., Nav. Med. Sch., Nav. Med. Center, Washington, D. C., for instruction.
KENNEDY, Thomas J., Lieut. Comdr., Washington, D. C., Naval Reserve Aviation Base, Anacostia, D. C.
McCARTHY, Lawrence J., Lieut. Comdr., Boston, Naval Hospital, Chelsea, Mass.; continue duty.
RICCIARDI, Ignatius J., Lieut. (j. g.), Milwaukee, Wisconsin and Upper Penninsula of Michigan, less the Superior area.
WIESINGER, Warren E., Lieut. (j. g.), Oakland, Calif., Receiving Ship, San Francsico.
WILSON, Merton Clarke, Lieut. Comdr., Detroit, Lower Peninsula of Michigan, plus Toledo area.
WIPPERMAN, Frederic F., Lieut. (j. g.), Minneapolis, Naval Reserve Air Base, Minneapolis.
WITWER, Russell G., Lieut. (j. g.), Cleveland Heights, Ohio, Northern part of Ohio, less Toledo area.

ORGANIZATION SECTION

OFFICIAL NOTES

ANNUAL CONGRESS ON MEDICAL EDUCATION AND LICENSURE

The thirty-seventh Annual Congress of the Council on Medical Education and Hospitals of the American Medical Association will be held at the Palmer House, Chicago, Feb. 17 and 18, 1941. Topics to be discussed include the place of the medical profession in the program of national defense, adjustment of medical education to social demand, coordination of professional education in medicine and allied fields, the teaching of public health and of surgery, education of Negroes, nomenclature, function of the museum in the medical school, a naturopathic subterfuge, and developments in the field of dental education. A tentative list of speakers follows:

Raymond Allen, M.D., Executive Dean, Professional Schools, University of Illinois, Chicago.
William Boyd, M.D., Professor of Pathology and Bacteriology, University of Toronto, Ontario.
C. Sidney Burwell, M.D., Dean, Harvard Medical School, Boston.
Oliver C. Carmichael, LL.D., Chancellor, Vanderbilt University, Nashville, Tenn.
Haven Emerson, M.D., formerly executive officer of the Delamar Institute of Public Health, Columbia University.
Rt. Rev. Maurice F. Griffin, LL.D., Trustee, American Hospital Association, Cleveland.
Samuel C. Harvey, M.D., Professor of Surgery, Yale University School of Medicine, New Haven.
Mr. J. W. Holloway Jr., LL.B., Acting Director, Bureau of Legal Medicine and Legislation, American Medical Association, Chicago.
Edwin P. Jordan, M.D., Assistant Editor, JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION, Chicago.
Chauncey Leake, Ph.D., Professor of Pharmacology, University of California Medical School, San Francisco.
Edward L. Turner, M.D., President, Meharry Medical College, Nashville, Tenn.
Lewis H. Weed, M.D., Chairman, Division of Medical Sciences, National Research Council, Baltimore.
Ray Lyman Wilbur, M.D., Chairman, Council on Medical Education and Hospitals, American Medical Association, Stanford University, Calif.

The Federation of State Medical Boards of the United States will participate in the congress, covering such subjects as basic science laws, the National Board of Medical Examiners as related to medical licensure, the status of the internship, the legal status of the physician and practice violators. Among the speakers will be:

Charles Carter, Ph.D., Chairman, Iowa Board of Examiners in the Basic Sciences, Fairfield.
Mr. E. S. Elwood, Executive Secretary, National Board of Medical Examiners, Philadelphia.
Reginald Fitz, M.D., Assistant to the Dean, Harvard Medical School, Boston.
I. D. Metzger, M.D., Chairman, Pennsylvania Board of Medical Education and Licensure, Pittsburgh.
Julian F. Du Bois, M.D., Secretary and F. Manley Brist, LL.B., Attorney, Minnesota Board of Medical Examiners, St. Paul.

Dr. Ray Lyman Wilbur, President of Stanford University, will be the guest speaker at the Annual Dinner of the Federation.

RADIO BROADCASTS

"Doctors at Work" is the title of the sixth annual series of dramatized radio programs being presented by the American Medical Association and the National Broadcasting Company.

The series opened Wednesday, November 13, and will run for thirty consecutive weeks, closing with a broadcast from the A. M. A. meeting at Cleveland on June 3, 1941. The program is scheduled for 10:30 p. m. eastern standard time (9:30 central, 8:30 mountain, 7:30 Pacific time) over the Blue network, other N. B. C. stations and Canadian stations.

These programs are broadcast on what is known in radio as a sustaining basis; that is, the time is furnished gratis by the radio network and local stations and no revenue is derived from the programs. Therefore, local stations may or may not take the programs at their discretion, except those stations which are owned and operated by the National Broadcasting Company.

Some radio stations may be unable to broadcast the program at the regular scheduled time and may transcribe and broadcast it at another hour or even on another day. It is advisable therefore to verify the time by reference to local newspapers or by telephoning the local Blue network stations.

The programs will dramatize what modern medicine offers the individual in the way of opportunities for better health and the more successful treatment of disease. Incidental to this main theme, the programs will explain the characteristics of the different fields of modern medicine and its specialties.

Descriptive posters for local distribution may be had gratis from the Bureau of Health Education, American Medical Association, 535 North Dearborn Street, Chicago. Program titles will be announced weekly in THE JOURNAL and monthly in *Hygeia*, the Health Magazine.

Tickets are available for each broadcast. Address the Bureau of Health Education, American Medical Association, 535 North Dearborn Street, Chicago. Tickets are free, but a stamped self-addressed envelop should accompany requests.

The next three programs to be broadcast, together with their dates and their topics, are as follows:

December 11. The Family's First Friend.
December 18. A Stitch in Time.
December 25. The Country Doctor.

ADDRESSES BY OFFICIAL STAFF

DR. W. W. BAUER:
Dec. 10—University of Michigan Public Health Assembly, Ann Arbor.
Dec. 13—Will-Grundy County Medical Society, Joliet, Ill.
Dec. 16—Wells High School, Chicago.

DR. MORRIS FISHBEIN:
Dec. 12—Allegany-Garrett County Medical Society, Cumberland, Md.
Dec. 12—Cumberland Forum, Cumberland, Md.
Dec. 15—Newton Community Forum, Newtonville, Mass.
Dec. 16—Merrill Institute and Free Lecture Association, Exeter, N. H.
Dec. 17—Pharmaceutical Advertising Directors Club, New York.
Jan. 3—Academy of Medicine of Toledo and Lucas County, Toledo, Ohio.

DR. FRANK H. LAHEY:
Dec. 10-12—Southern Surgical Society, Hot Springs, Va.
Dec. 16—Fulton County Medical Society, Atlanta, Ga.
Dec. 19—Gloucester County Medical Society, Woodbury, N. J.

DR. CARL M. PETERSON:
Dec. 19—Section on Industrial Health of the Philadelphia County (Pa.) Medical Society.

DR. PAUL A. TESCHNER:
Dec. 9—Y. M. C. A., Central Branch, Chicago.
Dec. 18—Lincoln Park Kiwanis Club, Chicago.

DR. NATHAN B. VAN ETTEN:
Dec. 7—Bronx Medical Association, New York.
Dec. 12—Linn County Medical Society, Cedar Rapids, Iowa.
Dec. 17—Monroe County Medical Society, Rochester, N. Y.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

ALABAMA

Personal. — Dr. Nicholas H. Dejanney, Detroit, has been appointed a member of the tuberculosis staff of the state department of health of Alabama.

Regional Meeting. — The Northwestern Division of the Medical Association of the State of Alabama met in Reform, October 10, with the following speakers: Drs. Frederick W. Wilkerson, Montgomery, "Cardiac Neuroses"; James S. Snow, Birmingham, "Drug Eruptions"; Joseph Alston Maxwell, Tuscaloosa (subject not announced); John W. Simpson, Birmingham, "The Child's Little Stomach," and David H. Wright, Berry, "Coronary Thrombosis."

CALIFORNIA

Symposium on Military Preparedness. — A symposium on military preparedness constituted the program of the Los Angeles County Medical Association at its meeting, November 7; the speakers were Judge Peirson M. Hall, selective service board; Rear Admiral David C. Cather, the navy, and Major John F. Bohlender, the army.

The Physician and the Military Emergency.—The San Francisco County Medical Society, San Francisco, devoted its meeting, November 12, to a symposium on "The Physician in Our Present Military Emergency." Dr. Philip K. Gilman, chairman of the state committee on medical preparedness, opened the meeting. Other speakers were Dr. Charles A. Dukes, Oakland, representing the selective service board; Dr. Herbert D. Crall, the army; Capt. Edward U. Reed, the navy, and Comdr. Clinton C. Defoney, the air corps.

FLORIDA

In Memory of Dr. Joseph Porter.—A housing project consisting of 136 family units will be called the Joseph Y. Porter Place to honor a physician who for many years before his death was state health officer. The project, named by the Key West Housing Authority, will be situated on recently purchased property on Trumbo Island, according to the state medical journal. Dr. Joseph Yates Porter graduated at Jefferson Medical College of Philadelphia in 1870 and in the same year was appointed assistant surgeon in the army. He was in charge of government relief measures during the yellow fever epidemic in Jacksonville in 1888 and was one of the first to support the mosquito transmission theory of yellow fever. He was appointed deputy surgeon general with the rank of lieutenant colonel and in 1907 was retired by Act of Congress. Among other positions, Dr. Porter served as quarantine inspector for the U. S. Public Health Service; president of the Florida Medical Association; for some thirty years state health officer; president of the state and provincial boards of health, 1909-1910, and camp surgeon at Camp Joseph E. Johnston during the World War. He was 79 years of age when he died, March 16, 1927.

ILLINOIS

District Meeting.—The Sangamon County Medical Society held a joint meeting with the District Medical Society of Central Illinois at St. John's Hospital in Springfield, November 7. Participating in the program were:

Dr. Sidney O. Levinson, Chicago, Serum Transfusions or Blood Transfusions?
Dr. Frederick A. Jostes, St. Louis, Manipulative Treatment of Backache.
Dr. Louis H. Jorstad, St. Louis, Surgery or Radiation in Cancer of Skin and Mouth.
Dr. Ralph H. Major, Kansas City, Mo., Changing Picture of Therapy in Pneumonia.
Dr. Thomas D. Masters, Springfield, Chronic Peripheral Artery Disease.
Dr. Robert J. Patton, Springfield, Endometrioma of Sigmoid with Obstruction.
Dr. Henry S. Dickerman Jr., Springfield, The Thyroid Heart.

Chicago

Gifts to Northwestern University.—Northwestern University has received $635,000 from the estate of the late Dr. John S. Appleman, it is reported; $135,000 is restricted to use of the medical school clinics. Announcement has also been made of a gift of $162,000 from the Clara A. Abbott trust for advancement of medical, chemical and surgical science. Mrs. Abbott, widow of Dr. Wallace C. Abbott, founder of the Abbott Laboratories in North Chicago, previously had given the university $1,500,000 for similar purposes. —— A gift of $50,000 from Miss Edith L. Patterson, Sterling, Ill., as additional endowment for the Patterson cancer clinic at Passavant Hospital, Northwestern University, was recently announced.

Society News. — The Chicago Urological Society was addressed, November 28, by Drs. Joseph H. Kiefer on "Tumors of the Testicle: Hormone Determinations in Diagnosis and Management"; Gustav Kolischer, "The Irritable Bladder," and Fay H. Squire, "Deep Roentgen Therapy in Elusive Ulcer of the Bladder: An Analysis of Twenty-Five Treated Cases."—— Dr. John Alexander, Ann Arbor, addressed a joint meeting of the Chicago Tuberculosis Society and the Illinois chapter of the American College of Chest Physicians, November 18, on "Management of Bronchiectasis."——The Chicago Laryngological and Otological Society was addressed, December 2, by Drs. Elmer W. Hagens on "Otosclerosis in Identical Twins" (case report) and Stuart C. Cullen, Iowa City, "Anesthesia in Otolaryngology."

INDIANA

State Medical Election.—Dr. Maynard A. Austin, Anderson, was chosen president-elect of the Indiana State Medical Association at its recent annual meeting in French Lick. Dr. Albert M. Mitchell, Terre Haute, will take office as president January 1. Indianapolis was selected as the place for the 1941 annual session.

Society News.—Dr. Thurman B. Rice, Indianapolis, discussed poliomyelitis before the Huntington County Medical Society, Huntington, October 2. —— The Fountain-Warren County Medical Society was addressed in Kramer, October 3, by Dr. Frank W. Cregor, Indianapolis, and Mr. Thomas A. Hendricks, Indianapolis, on "United Efforts of the Medical Profession."——Dr. Russell L. Haden, Cleveland, addressed the Tippecanoe County Medical Society in Lafayette, October 8, on "Pathologic Hemorrhage and Blood Dyscrasias." —— Dr. William F. King, Indianapolis, presented "Clinical Pictures of Blood Dyscrasia" before the Hendricks County Medical Society in Danville, October 24. —— Lieut.-Col. Robinson Hitchcock, on the staff of the adjutant general's office, state of Indiana, discussed "National Defense and the Indiana Selective Service Plan" before the Indianapolis Medical Society, November 12. Dr. Norman E. Freeman, Philadelphia, addressed the society, November 26, on "Peripheral Circulatory Failure: Its Prevention and Treatment."

MARYLAND

Joint Psychiatric Meeting. — The Maryland Psychiatric Society and the neuropsychiatric section of the Baltimore City Medical Society will hold a joint session at Towson, December 12. Dr. Max Levin, Baltimore, will speak on "Pathogenesis of Narcolepsy" and Dr. Lawrence F. Woolley, Towson, "Technic of Curare-Metrazol Therapy."

The De Lamar Lectures. — Johns Hopkins University School of Hygiene and Public Health announced the following program for the 1940-1941 series of De Lamar Lectures:

Dr. Virgil P. W. Sydenstricker, Augusta, Ga., November 19, Dietary Problems of the Southern United States.
Otto A. Bessey, Ph.D., Boston, November 26, Morphological Defects in Dietary Deficiency States.
George R. Cowgill, Ph.D., New Haven, Conn., December 3, Nutritional Deficiences in Tropical America.
Dr. Edward H. Hatton, Chicago, February 18, Etiology of Dental Caries.
Dr. Max Theiler, New York, March 4, Studies on Poliomyelitis.
Dr. Charles N. Leach, Montgomery, Ala., March 18, Recent Studies on the Epidemiology of Rabies.

MASSACHUSETTS

New Health Commissioner of Boston. — Dr. George Lynde Gately, Boston, has been appointed health commissioner of the city of Boston. He succeeds Dr. Henry F. R. Watts, who has retired on a pension after having served the city thirty-one years in different capacities. Dr. Gately graduated at Tufts College Medical School, Boston, in 1918. He is 46 years of age.

Society News.—Dr. Donald Ewen Cameron, Albany, N. Y., addressed the New England Society of Psychiatry, November 13, in Northampton on "Influence of the Times on the Teaching of Psychiatry."——Dr. Morris J. Nicholson, Boston, will speak on "Fractional Spinal Anesthesia" before the New England Society of Anesthesiology in Boston, December 10.

Dr. Albert H. Miller, Providence, R. I., addressed the society, November 12, on "Mechanics of Gas Anesthesia."——Among others, Dr. Francis S. Cheever, Boston, discussed "Observations on the Brown-Pearce Carcinoma in Roller Tile Tissue Cultures" before the Boston Society of Biologists, November 20.

MICHIGAN

Outbreak of Smallpox.—Two cases of smallpox have been reported in Detroit and 5 in Highland Park, newspapers announced November 16. These cases, the first reported in Detroit in three years, prompted Henry F. Vaughan, Dr.P.H., health commissioner, to urge all persons who have not been successfully vaccinated for smallpox within the last five years to have it done at once, it was said. There were 371 cases in the state in 1939 and 25 cases during the first eight months of 1940.

The Dr. Max Ballin Memorial Lectures.—The first lecture in the annual series sponsored by the North End Clinic, Detroit, in memory of Dr. Max Ballin was delivered, November 27, by Dr. August A. Werner, assistant professor of internal medicine, St. Louis University School of Medicine. His subject was "Recent Advances in Endocrine Therapy." The second lecture was given, December 4, by Dr. Walter C. Alvarez, Rochester, Minn., on "Recent Advances in Treatment of Food Allergy," and the last, December 11, will be by Dr. Harold J. Jeghers, Boston, assistant professor of medicine, Boston University School of Medicine, "Recent Advances in Vitamin Therapy."

NEW JERSEY

Society News.—Dr. Charles W. Mayo, Rochester, Minn., addressed the Bergen County Medical Society, Englewood, November 12, on "Surgical Treatment of Malignancy of the Right Colon."——Dr. Edward A. Strecker, Philadelphia, addressed the Camden County Medical Society, Camden, November 5, on alcoholism.——Dr. Edward Weiss, Philadelphia, addressed the Atlantic County Medical Society, Atlantic City, November 8, on "Recent Advances in Hypertension and Kidney Disease."——Dr. Tracy J. Putnam, New York, was the speaker at a joint meeting of the Academy of Medicine of Northern New Jersey and the New Jersey Neuropsychiatric Society, Newark, November 19, on "Surgical Treatment of Athetosis and Paralysis Agitans."——Dr. Waltman Walters, Rochester, Minn., addressed the Essex County Medical Society, Newark, November 14, on "Lesions of the Biliary Tract."

NEW YORK

Course on Diseases of the Chest.—The Rockland County Medical Society is presenting a course on diseases of the chest at the Summit Park Sanatorium, Pomona. The series is as follows:

Dr. Edgar M. Medlar, Mount McGregor, Pathogenesis of Tuberculosis: Clinical Interpretation, November 15.
Dr. William J. Ryan, Pomona, Pulmonary Tuberculosis: Early Diagnosis and Differential Diagnosis, November 22.
Dr. Edward Percy Eglee, New York, Tuberculosis of the Lungs and Pleura; Medical and Surgical Treatment, November 29.
Dr. Herbert C. Maier, New York, Suppurative Disease of the Lung: Suppurative Pneumonia, Abscess, Bronchiectasis, December 6.
Dr. Francis B. Berry, New York, Benign and Malignant Neoplasms: Diagnosis, Clinical Effects and Treatment, December 13.
Dr. Oswald R. Jones, New York, Fibrosis and Emphysema: Causes, Differentiation, Management, December 20.
Dr. John D. Kernan, New York, Bronchoscopy in Diseases of the Chest, December 27.

The course was arranged by the committee on public health and education of the Medical Society of the State of New York.

New York City

Roentgen Examination for Drafted Men.—The tuberculosis service project of the Works Progress Administration in conjunction with the bureau of tuberculosis of the New York City Department of Health is conducting roentgen examinations of prospective selective service draftees. Mobile x-ray units are set up in four armories to make a film of each man. The films will be developed and read during the period required for the physical examinations. Most of them can be finished within one or two hours. Any men who are found to have evidence of pulmonary disease will be followed up in the routine manner by the health department's bureau of tuberculosis.

Health Preparedness Committee.—Mayor La Guardia has appointed an official Advisory Health Preparedness Committee at the request of Assemblyman Lee B. Mailler, chairman of the New York State Health Commission. The committee has twenty-three physicians, nurses and officials of private and municipal health and welfare organizations. Among the membership are Drs. John L. Rice, health commissioner, and Willard C. Rappleye, commissioner of hospitals, representing the city; Claude W. Munger, the voluntary hospitals; George Baehr, the New York Academy of Medicine; Condict W. Cutler Jr., Harry P. Mencken, Flushing, Edward R. Cunniffe, Thomas A. McGoldrick, Brooklyn, and Arthur S. Driscoll, Staten Island, the five county medical societies. The committee is intended to function as a unit of the national defense program, operating in the public health field.

National Youth Administration to Examine Youth Employees.—A campaign of preventive medicine is being carried on among National Youth Administration youths between 18 and 24 years of age, consisting of physical tests and laboratory check-ups of the 13,000 National Youth Administration part time workers. The examinations are being conducted by the Medical Unit of the Astoria Work Experience Center, 43-02 Ditmars Boulevard, Astoria, L. I. This is the first time that medical examinations have been given youth employees by a medical unit of the National Youth Administration. In the past they have been conducted with the cooperation of various city hospitals and clinics. The examinations will cover first the youth personnel at the Astoria Center. Afterward those employed in the other centers and agencies will be brought in for tests. The medical unit is under the direction of Dr. Harold Jacobziner, assisted by seven physicians, five dentists, two dental hygienists, two nurses and a laboratory specialist. Persons showing the necessity of further treatment will be referred to the proper clinics. Frequent follow-up tests will be made by the medical unit to determine the progress in each case, and all examinations will be repeated annually. Through the cooperation of the New York City Department of Health, a portable x-ray machine will be provided for chest examinations of those young workers who show a positive reaction to the Mantoux tuberculin skin test. A vigorous campaign of health education will be carried on simultaneously with the medical program. Lectures, movies, dioramas and literature will be used. According to Dr. Jacobziner, the surveys will not show any definite results for some time. They will be carried on over a period of several years so that results may be tested and proved.

NORTH DAKOTA

"North Dakota Naturopathic Physicians, Inc."—Naturopaths must be licensed by a state board to practice in North Dakota, according to a decision handed down by Judge Daniel B. Holt, Fargo. The ruling was made in an action by the state board of medical examiners against "North Dakota Naturopathic Physicians, Inc.," a private corporation incorporated in 1938 for the stated purpose, among other things, of examining naturopaths and certifying as to their qualifications to practice in the state, according to the Grand Forks *Herald*. The corporation issued certificates to some of its members as "registered naturopathic physicians" and required that these certificates be filed with the register of deeds in the county in which the certificants resided, it was said. Judge Holt, in overruling a demurrer interposed by the corporation, said that, under the pleadings, the naturopaths sought to evade the laws of North Dakota and to do by indirection what they could not do directly, namely to engage in the practice of medicine without a state license. Judge H. A. Bronson, Grand Forks, represented the state board of medical examiners.

OHIO

Cleveland's Health Museum Opened.—The Cleveland Health Museum, first of its kind in the United States, was opened with a ceremony and civic luncheon November 12-13. Dr. James A. Doull, chairman of the advisory council of the museum, presided at the evening meeting. Official greetings were presented from local and national organizations and addresses were delivered by Drs. Howard Lester Taylor, president of the museum, on "From Idea to Museum in Four Years" and Bruno Gebhard, director, on "The Human Estate." Speakers at the luncheon, given by the Cleveland Chamber of Commerce were Mr. F. C. Crawford, president of the chamber of commerce, on "America's First Health Museum—Its Importance to This Community"; Mayor Harold H. Burton, "An Acknowledgement to Those Who Have Made the Museum Possible"; William J. Hutchins, LL.D., president emeritus of Berea College, Berea, Ky., "Health and National Defense," and Dr. William W. Bauer, director of the Bureau of Health Education, American Medical Association, Chicago, "Pictures of Health." The museum had its inception at a meeting of representatives of twenty-three institutions called by the Acad-

emy of Medicine of Cleveland, March 25, 1936. In December 1936 it was announced that Mrs. Francis F. Prentiss was willing to donate her former home at 8811 Euclid Avenue to the cause. During the past four years funds have been accumulated through memberships among the professions and several substantial donations. In May Dr. Gebhard, formerly curator of the Dresden Museum in Germany, was appointed director. During the summer the three story building was remodeled to provide display rooms, offices, workshops and auditorium. The opening display had 133 exhibits, most of which were made in the museum workshops.

OREGON

New Hospitals Opened. — The Blue Mountain General Hospital, a new building with a capacity of twenty beds, was opened at Prairie City in September. Dr. Oliver M. Nisbet, Portland, made an address on the progress of medicine and surgery at the opening ceremony.——A new county hospital and infirmary for Klamath County was dedicated October 13.

Medical Executives' Conference. — The fourth annual meeting of the Pacific States Medical Executives' Conference will be in Portland, December 8. Among subjects to be considered are medical military preparedness, coverage by insurance or other prepayment plans for families of low wage employee groups, the National Physicians' Committee for Extension of Medical Service, federal and state legislation and medical service plans.

Society News. — Speakers before the Multnomah County Medical Society, Portland, November 6, were Drs. Charles E. Gurney, on "Relationship of Plastic Surgery to Tumors of the Face"; William W. Baum, "Some Problems and Activities Confronting the Oregon State Medical Society"; Ralph A. Fenton, "National Problems of the Physician," and John H. Fitzgibbon, "Report of Activities of the House of Delegates of the American Medical Association."

PENNSYLVANIA

Psychiatric Meeting.—Dr. Baldwin L. Keyes, Philadelphia, was chosen president-elect of the Pennsylvania Psychiatric Society at its recent annual meeting in Philadelphia, and Dr. Henry I. Klopp, Allentown, became president. Dr. Leroy M. A. Maeder, Philadelphia, is secretary. Speakers on the program were Drs. Appleton H. Pierce, Coatesville, on "Mental Hygiene"; Samuel B. Hadden, Philadelphia, "Treatment of Neuroses by Class Technic"; Lauren H. Smith, Joseph F. Hughes and Donald W. Hastings, Philadelphia, "First Impressions of Electroshock Treatment in the Psychoses."

Philadelphia

Special Program.—The College of Physicians of Philadelphia presented a special program on medical preparedness, November 8. Francis John W. Roughton, lecturer in physiology at Cambridge University and a member of the British Committee on Blood Storage and Shock, spoke on "Blood Storage and Shock" and Lieut. Col. Arthur P. Hitchens, professor of public health and preventive medicine, University of Pennsylvania School of Medicine, discussed "A Health Program for the Home Side in War Time."

PUERTO RICO

Puerto Rico Medical Association. — The thirty-seventh annual meeting of the Puerto Rico Medical Association will be held in Santurce, December 12-15, under the presidency of Dr. Oscar G. Costa-Mandry, San Juan. Guest speakers will include:

Dr. Louis F. Bishop, New York, Coronary Disease—Its Diagnosis and Treatment.
Dr. Malcolm T. MacEachern, Chicago, Trends in Specialization in Medicine.
Dr. Warren F. Draper, assistant surgeon general, U. S. Public Health Service, Washington, D. C., subject not announced.
Mr. James A. Hamilton, director of New Haven Hospital, New Haven, Conn., Hospital Administration and the Various Methods of Securing Training.
Dr. Arthur C. Bachmeyer, Chicago, Relations Between Hospital Administrators and Members of the Professional Staff of the Hospital.
Mr. Rafael Picó, professor of geography, University of Puerto Rico, The White Man in the Tropics.

Puerto Rican physicians on the program include:

Dr. Jose C. Ferrer, San Juan, Renal Pain.
Dr. Jaime F. Pou-Valldejuli, Hato Rey, Pneumothorax in Patients of Middle Age.
Drs. Ramon M. Suarez and Enrique Koppisch, San Juan, Weil's Disease in Puerto Rico.
Dr. Ernesto Quintero, San Juan, Control of Venereal Diseases.
Dr. Rafael Lopez Nussa, San Juan, Treatment of Uterine Cancer.

GENERAL

Deaths from Football Decline.—Eight deaths attributable to football occurred during the first half of this year's season, according to a report by Floyd R. Eastwood, Ph.D., Purdue University, Lafayette, Ind., record keeper for the American Football Coaches and National Collegiate Athletic associations. Five deaths resulted directly from football, two less than in 1939. Two boys died of heart disease and one from an infection. The toll has shown a downward trend since 1937, Dr. Eastwood reported.

Association for Study of Neoplastic Diseases. — The annual meeting of the American Association for the Study of Neoplastic Diseases will be held at Johns Hopkins Hospital, Baltimore, December 19-21. The meeting will consist of demonstrations of microscopic pathology and of roentgenograms and lantern slides. Session topics and chairmen will be:

Dr. Alexander M. Duff Jr., Baltimore, Lesions of the Nasopharynx, Larynx, Trachea and Upper Respiratory Tract.
Dr. Leopold Clarence Cohn, Baltimore, Lesions of the Breast.
Drs. Louise D. Larimore, Greenwich, Conn., and Georgeanna Seegar Jones, Baltimore, Lesions of the Female Genital System.
Drs. George S. Foster, Manchester, N. H., and William A. Wall, Cortland, N. Y., Lesions of the Endocrine Glands.
Dr. Howard H. Ashbury, Baltimore, Lesions of Bone.
Dr. Roscoe W. Teahan, Philadelphia, subject not announced.
Drs. George A. Stewart and Sam S. Blackman Jr., Baltimore, Lesions of the Lymphoid, Myeloid and Reticulo-Endothelial Systems.

Changes in Status of Licensure. — The Colorado Board of Medical Examiners reports the following action:

Dr. William Ewell Montgomery, Pueblo, license revoked, October 1, for conviction of a felony.

The Florida State Board of Medical Examiners reports the following action:

Dr. Eldridge Roy Morlan, Auburndale, license revoked, June 8, for falsifying an affidavit.
Dr. Scott Robert Edwards, now of New York, license revoked, June 8, for violation of Harrison Narcotic Law.
Dr. Charles Russell Conway, alias Charles Wade Page, Chipley, license revoked, June 8, because of conviction of stealing an automobile and serving a sentence at the state prison at Raiford.

The Illinois State Department of Registration announces the following action:

Dr. Archibald B. Calvin, Chicago, license restored, September 23.

The Maine Board of Registration of Medicine announces the following:

Dr. Henry B. Esmond, Casco, license revoked, July 2, for obtaining fraudulently his license to practice medicine.

The Massachusetts Department of Registration in Medicine announces the following action taken July 11:

Dr. Anthony Peter Carogana, Chelsea, license revoked for his conviction on charge of performing an abortion.

The South Dakota state board of health and medical examiners announces the following action:

Dr. George E. Johnson, Gregory, license revoked, July 16, for unprofessional conduct.

Squibb Award in Endocrinology.—To promote interest in research dealing with endocrinology, E. R. Squibb & Sons have established an annual award of $1,000 to be given through the medium of the Association for the Study of Internal Secretions, according to *Science*. The award will be given to the research worker in the United States or Canada who, in the opinion of the judges, has published during the previous calendar year the most meritorious scientific report dealing with the field of the hormones. While it will be given primarily for publication of specific papers, the judges will be given latitude in the exercise of their function. If in their judgment circumstances and justice dictate, it may be recommended that the prize be divided between two or more persons. It may also be recommended that it be made to a worker for valuable contributions over an extended period, but not necessarily representative of a given year. Membership in the association is not a requisite of eligibility for the award. A committee consisting of five members of the association will be appointed annually by the president to recommend to the council a recipient for the award. Nominations should be sent to the secretary of the association not later than January 15 for presentation at any given spring meeting. All details concerning the nominee will be considered confidential until the announcement is made at the annual dinner, when the award will be presented. While the award is intended as an annual prize, it will be withheld in accordance with the judgment of the awarding committee. In addition to the award provided by E. R. Squibb & Sons, the recipient will be presented with a simple scroll as a memento of the association, the cost to be defrayed by the association.

Foreign Letters

LONDON

(From Our Regular Correspondent)

Nov. 9, 1940.

London Hospitals Carry on During Bombardment

The London hospitals are in the battle zone, nearer to war operations than many a field hospital in past campaigns. Many have suffered severely from bombing and one great hospital of a famous medical school has had to be evacuated, but it carries on. The history of this war will show that in Britain's heroic struggle to save herself and Europe from the new barbarism, none deserve more praise for their work and courage than the hospital staffs—medical, nursing, clerical and domestic. Exposed to bombardment day and night and sometimes even when suffering from it, they carry on not only the usual service for the sick but a well organized system for dealing with the casualties of air raids. There is an elaborate air raid precautions service with a control room and roof watchers. The latter were introduced into factories, so that after an air raid warning work could be carried on until the danger came too near. Facilities are established for carrying on in the subbasements of hospitals when the higher parts become dangerous. Here are beds to which patients in the upper floors can be removed. At nights the subbasement is a sanctuary and haven of rest for those not on duty at the time.

The medical and nursing staffs have to be on the alert every night, for then attacks from the air are much more severe than by day. The casualties are received at a special ambulance entrance and taken to a hall where they are sorted. Persons not severely injured are treated at once; the others are taken to the wards. If the upper floors have been put out of action, an emergency operating room below ground is available.

Following is an example of the courage of our hospital staffs: In southeastern England high explosive bombs cut through the kitchen quarters of a hospital, damaging wards on both sides, killing one nurse, injuring five members of the staff and causing death from shock of several elderly patients. Immediately after the bombing the nurses on duty, medical students and porters set to work to remove the patients from the damaged wards to other parts of the building. They worked while the German bombers were still overhead and splinters from antiaircraft shells were falling. The majority of the nurses were young probationers under the age of 18, who carried on with a coolness and courage to which words cannot do justice.

Casualties from Bombing of the Civilian Population

In the House of Commons Mr. Churchill stated that the Germans claimed that on the night of October 3 they dropped 251 tons of high explosives on London. On that night it took 1 ton to kill three fourths of a person. In the last war the small bombs of earlier pattern which were used killed ten persons for every ton dropped on built-up areas. Therefore the deadliness of the bomb attack on civilians in this war appears to be only one thirteenth of that in the last war. The only explanation was the vastly improved methods of shelter. When we entered this war we expected losses which might amount to 3,000 killed in a single night and 12,000 wounded night after night. We had made hospital arrangements for 250,000 casualties but up to the present as the result of air bombing we had about 8,500 killed and 13,000 wounded. Since the heavy raiding began on September 7 the figures of killed and wounded had declined steadily from over 6,000 in the first week to just under 5,000 in the second, about 4,000 in the third and under 3,000 in the last four weeks. These are casualties—dead and seriously wounded. Mr. Churchill foreshadowed new methods of making the wholesale bombing of the civilian population "more exciting to the enemy than it is at present," but of course he would not describe them. "It would be much better for our visitors to find them out for themselves." We must try to have as soon as possible shelters with sleeping bunks for every one in the areas liable to constant attack. Measures were being taken to secure the health of the people under these novel and primordial conditions. The official figures for the casualties in air raids during the month of September are 6,954 civilians killed and 10,615 seriously injured.

The National Health Improves Under War Conditions

In the House of Commons the Minister of Health, Mr. Malcolm MacDonald, gave a survey of the health of the nation under war conditions. He deprecated the superficial view that health services were a prime concern in peace but in war were of secondary importance, while energy was concentrated on the production of munitions. But at the machines stood hosts of men and women whose health was of crucial importance. The health of the nation was on the march and not even the calamity of war could stay it. The health statistics for 1939, in which there were eight months of uneasy peace and four months of war, were almost uniformly better than those of the preceding year, which in turn were an advance. In 1939 50 per thousand children born died before their first birthday. That was the lowest figure ever recorded and was 3 per thousand less than in 1938. It was less than half the figure for 1914, the first year of the first world war. The second significant index was the maternal mortality. This fell to 2.82 per thousand births in 1939, which was also the lowest figure ever recorded in the country and was 0.15 below the previous year and little more than two thirds of the figure for 1914. The death rate for tuberculosis did not show any decline, but the figure was encouraging. The crude death rate in 1939 from all forms of tuberculosis was 636 per million living. That was 1 per million higher than in 1938 but less than half the figure for 1914. Only one case of smallpox was notified in 1939, the figures for scarlet fever and diphtheria were lower than those of 1938, and the anticipated biennial measles epidemic failed to appear. But our health chart was not uniformly good. There was an ominous increase in the incidence of cerebrospinal fever. The disease, however, was less formidable, thanks to sulfapyridine, which had reduced the mortality by almost two thirds.

American Vans for Blood Transfusion

The Medical Research Council has received four motor vehicles equipped for medical work from the United States. They were originally purchased by the American Quakers and the International Commission for the Assistance of Child Refugees for use in France. They will now be used principally for the work of the Emergency Blood Supply depots in the neighborhood of London.

Marriages

BARCLAY MILLER BRANDMILLER, Youngstown, Ohio, to Miss Jean Elizabeth Richards in Struthers, September 19.

ROLAND SIGURD ARONSON, Philadelphia, to Miss Catherine Reimann Roess of Oil City, Pa., August 31.

EMORY HAMLIN ANDERSON, Paia, Hawaii, to Miss Janice Watkins of Oakland, Calif., August 21.

MAURICE MILTON FLIESS, Clifton Forge, Va., to Miss Irwin Rand Foster of Lynchburg, August 3.

JOSEPH NEGLEY SCHAEFFER, Dayton, Ohio, to Miss Sarah Jane Bradshaw of Bexley in August.

BEN E. EWING to Miss Mary Kline, both of Madison, Neb., June 26.

Deaths

Oliver Thomas Osborne ✠ New Haven, Conn.; Yale University School of Medicine, 1884; member of the House of Delegates of the American Medical Association in 1902, 1903 and 1908 and member of the Council on Pharmacy and Chemistry from 1910 to 1916; vice president from 1910 to 1920, and delegate to the United States Pharmacopeial Convention and member of the revision committee; president of the New Haven County Medical Association in 1899 and the American Therapeutic Society in 1905; fellow of the American College of Physicians; instructor of materia medica and therapeutics, 1891-1892, assistant professor of materia medica and therapeutics from 1892 to 1895, professor of materia medica and therapeutics from 1895 to 1906, professor of materia medica and therapeutics and clinical professor of medicine from 1906 to 1911, professor of therapeutics from 1911 to 1922, clinical professor of therapeutics from 1922 to 1925 and since 1925 clinical professor emeritus at his alma mater; one of the founders and chairman of the medical board of the Gaylord Farm Sanatorium, Wallingford, Conn., from 1903 to 1940; received the first Chompret Prize of the International Academy of Stomatology, in cooperation with the American Society of Stomatologists in 1933; editor of the "Section on Therapeutics" of THE JOURNAL from 1907 to 1919; author of "Introduction to Materia Medica and Pharmacology," 1906; co-author with Dr. Morris Fishbein of "Handbook of Therapy," 1910, ninth edition 1933; author of "Prevention and Treatment of Infections," 1915, "Disturbances of the Heart," 1916, third edition 1925, "Disturbances of the Kidneys," 1917, "Principles of Therapeutics," 1921, "What Everyone Ought to Know," 1929, "Mouth Infection," 1934, and "The Evaluation of Symptoms," 1935; section on "Acromegaly" in Buck's "Reference Handbook of the Medical Sciences," 1893, and "Organotherapy" in Cohen's "System of Physiologic Therapeutics," 1905, and more than 100 articles in medical periodicals; aged 77; died, November 11.

William Gooderham Cameron, Tacoma, Wash.; University of Pennsylvania Department of Medicine, Philadelphia, 1897; member of the Washington State Medical Association, American Academy of Ophthalmology and Otolaryngology and the Pacific Coast Oto-Ophthalmological Society; fellow of the American College of Surgeons; past president of the Pierce County Medical Society and the Puget Sound Academy of Ophthalmology; formerly member of the state legislature; at one time health officer of the village of Staples, Minn.; ophthalmologist and otolaryngologist, Northern Pacific, Tacoma General and St. Joseph's hospitals; editor of the *Bulletin of the Pierce County Medical Society;* aged 66; died, October 23, of coronary occlusion.

George Mason Magruder ✠ Senior Surgeon, United States Public Health Service, Shadwell, Va.; University of Virginia Department of Medicine, Charlottesville, 1884; was commissioned an assistant surgeon in the United States Marine Hospital, later known as the United States Public Health Service, April 24, 1886, promoted to passed assistant surgeon Aug. 4, 1890, to surgeon Aug. 5, 1899, to senior surgeon Aug. 11, 1917, and retired Aug. 13, 1927; aged 77; died, October 10, in the University of Virginia Hospital, Charlottesville, of acute myelogenous leukemia.

Robert George Cook ✠ Canandaigua, N. Y.; College of Physicians and Surgeons, medical department of Columbia College, New York, 1889; member of the American Psychiatric Association; at various times neurologist, St. Mary's Hospital, Rochester, attending neurologist, Rochester City Hospital, consulting neurologist, Rochester State Hospital, director of the Frederick Ferris Thompson Memorial Hospital; consulting physician and treasurer and formerly physician in charge of the Brigham Hall Hospital; aged 76; died, October 25, of coronary occlusion.

Paul Tonnel Dessez ✠ Medical Inspector Commander, United States Navy, retired, Waterford, Conn.; Georgetown University School of Medicine, Washington, D. C., 1897; was commissioned an assistant surgeon in the navy June 20, 1903; veteran of the Spanish-American and World wars; was retired for disability on Dec. 1, 1922; received the Distinguished Service Medal, the Navy Cross, the Croix de Guerre and the Purple Heart; fellow of the American College of Surgeons; aged 64; died, August 29.

George Michael Jennings ✠ Missoula, Mont.; University of Minnesota College of Medicine and Surgery, Minneapolis, 1907; past president of the Medical Association of Montana and of the Montana State Board of Health; member and past president of the state board of medical examiners; fellow of the American College of Surgeons; chief surgeon of the Northern Pacific Beneficial Association Hospital; on the staff of St. Patrick Hospital; aged 60; died, October 14.

Henry Jackson, Brookline, Mass.; Harvard Medical School, Boston, 1884; member of the Massachusetts Medical Society and the Association of American Physicians; formerly instructor in clinical medicine at his alma mater; for many years on the staff of the Boston City Hospital; aged 81; died, October 4, of coronary thrombosis.

Charles Edward Boynton Jr. ✠ Atlanta, Ga.; Emory University School of Medicine, Atlanta, 1931; on the staff of the Crawford W. Long Hospital; aged 39; died, September 25, of estivo-autumnal malaria and chronic amebiasis.

Charles Miller Glassmire, Philadelphia; Medico-Chirurgical College of Philadelphia, 1914; on the staff of the American Hospital for Diseases of the Stomach; aged 53; died, October 7, of coronary thrombosis and angina pectoris.

William T. Highberger, Maysville, W. Va.; University of Maryland School of Medicine, Baltimore, 1883; member of the West Virginia State Medical Association; aged 80; died, September 6, of hemiplegia and arteriosclerosis.

Mary Margaret Johnson, Spokane, Wash.; Cleveland Homeopathic Medical College, 1898; member of the Washington State Medical Association; aged 76; died, October 20, in Sumner of cardiorenal vascular disease.

Hugo Emil Nelson, Sharon Springs, Kan.; John A. Creighton Medical College, Omaha, 1902; member of the Kansas Medical Society; aged 69; died, September 2, in the Mercy Hospital, Denver, of carcinoma of the prostate.

Newton Howard Jenkins, Kingston, Pa.; Hahnemann Medical College and Hospital of Philadelphia, 1905; aged 57; died, October 5, in the Robert Packer Hospital, Sayre, of polycystic kidney and heart disease.

Arthur Burnham Johnson, Toledo, Ohio; Rush Medical College, Chicago, 1928; for many years on the staff of the Women's and Children's Hospital; aged 43; died, October 3, of injuries received in a fall.

Cecil Norbert Brady, Newton, Mass.; Tufts College Medical School, Boston, 1913; served during the World War; aged 53; died, October 23, in the United States Naval Hospital, Chelsea, of heart disease.

Willis Sylvester Cobb, Corning, N. Y.; Albany Medical College, 1890; for many years county coroner; aged 78; died, October 5, in the Veterans Administration Facility, Bath, of coronary heart disease.

Lloyd Ephraim Strohm, Philadelphia; Hahnemann Medical College and Hospital of Philadelpia, 1916; aged 57; died, September 28, at Audubon, N. J., of acute cardiac dilatation and myocarditis.

Stephen Shaffer Landis ✠ Harrisburg, Pa.; University of Pittsburgh School of Medicine, 1911; for many years member of the school board; aged 53; died, October 1, of coronary occlusion.

William Edward Barton, Bethalto, Ill.; Barnes Medical College, St. Louis, 1909; formerly health officer of Wood River; aged 60; died, October 15, in Roxana of carcinoma of the stomach.

Anita Newcomb McGee, Washington, D. C.; Columbian University Medical Department, Washington, 1892; aged 76; died, October 5, of arteriosclerosis and cerebral hemorrhage.

Carl V. Cruse, Ioia, Ill.; Barnes Medical College, St. Louis, 1899; member of the Illinois State Medical Society; aged 67; died, October 12, of cardiorenal disease and arteriosclerosis.

Avington Adam Edgington, Omaha; State University of Iowa College of Medicine, Iowa City, 1897; aged 75; died, October 3, of paralysis agitans and hypostatic pneumonia.

Randolph Brunson, West Orange, N. J.; Medical Department of Tulane University of Louisiana, New Orleans, 1888; aged 75; died, September 25, of cerebral hemorrhage.

James F. Gullett, Hot Springs National Park, Ark. (licensed in Arkansas in 1903); aged 76; died, October 1, in St. Joseph's Hospital of bronchopneumonia.

Elliott H. Burnett, Rockford, Iowa; State University of Iowa College of Homeopathic Medicine, Iowa City, 1893; aged 85; died, October 1, of bronchopneumonia.

John M. Howard ✠ Amesville, Ohio; Starling Medical College, Columbus, 1895; aged 77; died, October 10, of injuries received in an automobile accident.

Hiram A. Castleberry, Ben Wheeler, Texas; University of Louisville (Ky.) Medical Department, 1895; aged 78; died, October 14, of gastric carcinoma.

Correspondence

DRUGS IN GREAT BRITAIN

To the Editor:—A note in *Science* of October 25, page 373, calls attention to the fact that important changes in medical prescribing in Great Britain are recommended by an official medical committee. Among the drugs said to be "in frequent use" and which are now hard to obtain are balsam of tolu, buchu leaves, calumba root, black catechu, gelsemium root, jalap and seneca root. Why these and many other antique galenicals and proprietary remedies are still used by British physicians is difficult to understand unless it is on the basis of steadfast British tradition. If the present war has no other good effect, it may at least serve to renovate some time worn habits in British therapeusis.

HOBART A. REIMANN, M.D., Philadelphia.

NOTE.—The Epitome of the Pharmacopeia and National Formulary, 1940 edition, published under the authorization of the Council on Pharmacy and Chemistry of the American Medical Association, makes the following succinct comments concerning these substances:

Balsam of Tolu. Used chiefly in the form of the syrup, which is little more than a pleasantly flavored vehicle.

Buchu. At one time largely used as a diuretic, especially in catarrhal cystitis. Value doubtful.

Calumba. Used as a simple bitter and stomachic. It appears to have no advantage over other bitters, such as gentian, except that it is free from tannin.

Gambir (Pale Catechu). Astringent; used against diarrhea in form of tincture.

Gelsemium. Used in migraine and neuralgia, and in the treatment of rheumatic, or ovarian and uterine pain. Efficacy uncertain. Untoward symptoms sometimes result from comparatively small doses.

Jalap. Drastic hydragogue cathartic, used especially in dropsies.

Seneca snake root. Employed as a nauseant expectorant (by virtue of the irritant saponin).

None of the foregoing are described in the U. S. Pharmacopeia, nor are the preparations accepted for inclusion in N. N. R.; they are not mentioned in Useful Drugs. They belong to those listings of drugs which are in the twilight of their existence.

The point raised by Dr. Reimann is well taken. It may be, however, that our English friends are more accustomed to the use of these drugs and therefore the lack of them may mean a hardship to those so accustomed.—ED.

MEN NURSES SUGGESTED FOR AMBULANCE DUTY

To the Editor:—In THE JOURNAL November 2 under Current Comment the questionable shortage of interns is discussed, and reference is made to the amount of time that the intern has to spend on ambulance duty. It was suggested that nurses or orderlies might be assigned to the more routine ambulance duties, such as transfer of patients.

In New York City two of the public hospitals have men nurses on the psychiatric ambulances. For the record I will say that in New York State, at least, men nurses are readily available, have had sound courses of training in medical, surgical, urologic and psychiatric nursing and are duly examined by the Bureau of Nurse Examiners and licensed by the University of the State of New York.

As secretary of the Men Nurses Section of the New York State Nurses Association and chairman of the program committee of the Men Nurses Section of the American Nurses Association, I would greatly appreciate any publicity or notice which your publication would give to the use of men nurses on ambulance duty. The man nurse is physically suited to the duty, and his professional training has prepared him to accept responsibility and to use judgment. While the salary of the man nurse is from $105 to $135 a month, he would release the interns for the duties which they expect.

The Men Nurses Section of the American Nurses Association has available considerable information on the national distribution of men nurses which it would gladly furnish to any employers who are seeking men nurses for this work.

NATHANIEL H. WOODING, R.N., Brooklyn.
Secretary, Men Nurses Section, New York State Nurses Association.

TRIBUTE TO PROFESSOR WENCKEBACH

To the Editor:—With the sad announcement of the death of Prof. Karel F. Wenckebach in Vienna recently there comes to a dramatic close one of the most brilliant epochs of contemporary medicine. His passing will bring sorrow to hundreds of American physicians who enjoyed the rare privilege of basking in the warm friendship of the great group of medical scientists who made Vienna during the nineteen twenties the shrine of postgraduate teaching.

It was here at the Wenckebach Clinic that modern cardiology was born; one by one the great lights of pioneer medical thought have gone out, and all the illustrious figures who strode across the stage of the clinic platform have disappeared. Through the doors of the American Medical Association of Vienna many doctors made lasting friendships with these teachers, and all of us will recall for a long time to come the pleasant memories of this group with their special little eccentricities:

Wenckebach himself, of military mien, a little out of place, perhaps, in the gemütlich atmosphere of Vienna, stern, dogmatic but kindly and a true clinician. To him angina pectoris was not a disease entity but only a symptom and until the death of Mackenzie was the latter's chief antagonist.

Heinrich Winterberg, quiet, calm, studious, the liaison member between the clinician Wenckebach and the laboratory experts. The clinical interpreter of the science of electrocardiography and the defender of Waller, the "forgotten man" of English cardiology.

Charles F. Rothberger, hard of hearing, the technical expert of the laboratory and the originator of experimental animal research in the understanding of electrocardiography, eager, enthusiastic, a brilliant mathematician and inventor of complicated apparatus in the study of electrodynamic phenomena of the beating heart.

Jacob Pal, elder physician of the group interested in the physiology of the circulation, classifier of diseases of the arteries, inventor of the modern blood pressure apparatus, exponent of arteriosclerosis.

Rudolph Kaufmann, the American postgraduate student's personal physician, exponent of the great family doctor. A cardiologist of many specialties, brilliant diagnostician.

Theodore Meyer, pharmacologist, research worker in glyceryl trinitrate, who developed the theophylline compounds, now called aminophylline, for the relief of stenocardial symptoms, early assayer of digitalis, biochemist largely responsible for the development of the mercurial diuretics, a charming personality.

Jacob Erdheim, pathologist extraordinary, the lordly clinical ruler of the postmortem table, at whose feet sat hundreds of enthralled American students who saw dead organs alive again and the heart reliving its last episode.

Wilhelm Neumann, the thoracic clinician to whom the sounds of the heart and lungs spoke in unmistakable terms, exponent of the phonetic method of teaching and demonstrator of many physical signs in the chest.

Finally, Julius Wagner-Jauregg, dean, stern, a strict disciplinarian albeit a kindly man, perpetually astonished at the ingenuity of American excuses, sincere advocate of academic freedom for medical research, later Nobel prize winner in medi-

cine. Anticipated instinctively, perhaps, the fate of Austria and sincerely believed that the torch of scientific medicine would eventually burn brightest in the United States.

And now the school is closed; the doors are shut and the last light has gone out. All those of us privileged to have known these men will cherish the memory of the Viennese school of medical leadership which flourished from 1920 until about 1928, and to every one who knew him the passing of the chief himself, Wenckebach, must call forth wistful thoughts of a medical era now definitely gone.

ALBERT S. HYMAN, M.D., New York.
President, Alumni Society of the American Medical Association of Vienna.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

NICOTINIC ACID FOR TOXIC MANIFESTATIONS OF SULFANILAMIDE

To the Editor:—**In The Journal for March 2, 1940, page 756, Dr. Doughty reported the successful treatment of certain toxic manifestations of sulfanilamide with nicotinic acid. A pharmaceutic house has asked if there is sufficient evidence to warrant the inclusion of nicotinic acid in a tablet of sulfanilamide. As this is not mentioned in the recent paper by Dr. Long, I am wondering whether such a combination would be justifiable?**

M.D., Canada.

ANSWER.—The available data concerning the use of nicotinic acid in preventing the toxic manifestations which may arise in the course of sulfonamide therapy are contradictory. Certain observers have reported that large doses of nicotinic acid (from 200 to 400 mg. a day) will decrease nausea and vomiting, cyanosis and other toxic manifestations of sulfanilamide therapy. Since McGinty's original report on this subject (McGinty, A. P.; Lewis, G. T., and Holtzclaw, M. R.: *J. M. A. Georgia* **28**:54 [Feb.] 1939), an attempt has been made in the Johns Hopkins Hospital to evaluate nicotinic acid in the prevention of the toxic manifestations which arise in the course of therapy with sulfanilamide and its derivatives. In certain cases it has seemed that the administration of nicotinic acid decreased nausea and vomiting, cyanosis, and the like, while in other cases treatment with nicotinic acid has had absolutely no effect on the toxic reactions of sulfanilamide. Because completely satisfactory methods of evaluating nicotinic acid deficiency states in human beings are not available, it has been impossible to determine whether the apparent good results from combined therapy in certain cases resulted from the abolishment of a deficiency state. At the present time the proposed combination of nicotinic acid with sulfanilamide in tablet form would not appear to be based on sound clinical observations.

HYPOGONADISM IN BOY

To the Editor:—**What is the present treatment of hypogonadism in a youth 17 years old who is in perfect health and mentally alert and who shows absolutely no evidence of secondary sex characteristics? Will you please discuss the probability of improvement and the likelihood of permanence of results?**

L. C. Howe, M.D., Muscatine, Iowa.

ANSWER.—It is assumed that gross pituitary disease has been ruled out as far as possible by x-ray examinations of the skull and visual fields. This step is necessary whether the patient has suggestive complaints or not. The essential defect may lie in the pituitary body or in the testes. Large amounts of follicle stimulating material may be found in the urine if the defect is gonadal, but the technics for its best measurement are as yet not agreed on and are not available for those without the services of a research laboratory. The results of treatment may answer this question. Pregnancy urine extract 500 international units three times weekly may be administered for a period of from four to six months, the results judged by a photographic record of progress. This dose should be achieved by graded steps and may even be doubled if well tolerated. If the response is satisfactory, treatment should be continued; if none is secured, the testes must be regarded as refractory and androgens used. Testosterone propionate 25 mg. intramuscularly three times weekly will usually produce unmistakable results in from three to four months or less. Androgenic and gonadotropic therapy are substitutional and regression of sex development may be expected if the patient is eunuchoid or suffers from pituitary dysfunction. This may be a case of delayed puberty in which the prognosis for normal sexual development is good.

FORMALDEHYDE POISONING

To the Editor:—**I should like to know the possible symptoms and signs found in people working with formaldehyde. A patient complains of weakness, dizziness and tingling of the fingers and nervousness and loss of weight. Physical examination gives negative results. Urinalysis is negative. The electrocardiogram is essentially normal. Blood examination reveals erythrocytes 4,710,000, hemoglobin 14 Gm., color index 0.96, leukocytes 8,800. The differential count is essentially normal.**

Earl Herron, M.D., Chicago.

ANSWER.—The characteristic manifestations of industrial formaldehyde poisoning are conjunctivitis, coryza, bronchitis, dermatitis, increased sensitivity of the skin in the absence of dermatitis, dizziness and feeling of great weakness. These symptoms appear in mild acute cases resulting from inhalation of the formaldehyde gas and in the case of cutaneous lesions direct contact with formaldehyde in solution. More prolonged involvement intensifies these lesions and in addition there may appear the symptoms of kidney irritation such as anuria, softened, necrotic fingernails, gastro-enteritis, rarely bronchopneumonia, hepatitis, anorexia, sleeplessness and palpitation.

The symptoms mentioned are compatible with the diagnosis of formaldehyde injury, but one could expect concomitant signs of irritation of the eyes, the upper and lower respiratory tract or the skin.

NAUSEA AND VOMITING FROM GENTIAN VIOLET PILLS

To the Editor:—**I am treating a family infected with pinworms—Oxyuris vermicularis—with gentian violet pills, according to the routine described in The Journal, June 8, 1940. I find nausea and vomiting so severe that carrying out the routine is impossible. Is there a way of overcoming this?**

M.D., Connecticut.

ANSWER.—Nausea and vomiting and even diarrhea may occur during the oral administration of gentian violet. These symptoms quickly subside on withdrawal of the drug.

The use of a coated tablet that does not disintegrate in the stomach is advised since not only is less gastrointestinal irritation produced but the effectiveness against oxyuriasis is enhanced. The diet should contain a moderate amount of roughage, fatty foods should be avoided and alcohol should be interdicted. It may be necessary to reduce the dosage or even to stop the drug for from twenty-four to forty-eight hours and continue the treatment with the maximum dose that is tolerated without unpleasant symptoms. In these instances it is recommended that the period of treatment be extended so that the total calculated dose is taken. Small doses of bismuth subnitrate may aid in allaying gastrointestinal symptoms.

PROPHYLACTIC VACCINATION FOR UNDULANT FEVER

To the Editor:—**There have been a number of scattered cases of abortus fever among cows in this region; there have also been occasional cases of human infection. Veterinary men "vaccinate" cows against this. The situation is better now. We medical men use the vaccine for therapeutic purposes when needful. I have seen no reports in The Journal of the use of vaccine for prophylactic purposes and write to inquire: In the presence of an endemic or partial epidemic situation, when individuals have used milk from infected cows without pasteurization (and without boiling) what doses of the vaccine should be given? How long does it take for immunity to be thus established? How often or at what intervals should the doses be given and should such doses be graduated upward progressively? Is it possible to obtain immunity by any means before the end of the incubation period of the trouble is reached in man? Are there any antitoxins known or on the market? If a family has been continuously using the milk from a cow now suspected to have had the trouble for one and one-half years past have they probably not developed a certain amount of immunity? Can an intensive short course of vaccination be put in operation by using short intervals between injections? I have used with success the combination of sulfanilamide and vaccine.**

Matthew Karasek, M.D., Shidler, Okla.

ANSWER.—Prophylactic vaccination of human beings against Brucella infection has not been studied on a scale sufficient to demonstrate its value. The fact that serum agglutinins may appear in relatively high titer following a cutaneous test with diluted Brucella vaccine or brucellergin in presumably normal individuals points to the possibility that protection might be afforded by vaccination. There is need for controlled studies in this field.

POLYNEURITIS OF PREGNANCY

To the Editor:—Is there evidence to show that parenteral administration of thiamine or liver extract would be more effective than oral administration? What would be considered effective treatment for a case of polyneuritis of pregnancy? How long should intensive vitamin therapy be continued before abandoning it as ineffective? The patient in question is a well nourished woman with myopia. The stated age is 36, the apparent age 50 years. There have been grand mal seizures since chorea at about 11 years. They have been controlled the past three years with phenobarbital 0.1 Gm. daily. She is a septipara, entirely normal except for the last recent gestation, which began with severe vomiting, dyspnea on slight exertion and irregular pulse. Although I feared for her life, she easily delivered a 9 pound (4,000 Gm.) infant, after which a moderate edema rapidly cleared away. For the past two years she has had rather severe left sciatic neuritis, in the hope of curing which all teeth were futilely removed. After delivery this pain was still annoying her but in addition she complained of numbness and tingling of both legs, more on the left. The proprioceptive sense in the feet and toes has decreased but is not gone. The knee jerks were exaggerated about the tenth postpartum day but now two months later they are only faintly active. Now (two months post partum) Romberg's sign is negative. The finger to nose test is normal on both sides. There is staggering gait, which is seemingly due to weakness. She turns her ankles frequently. The pupils react sluggishly to light. Her tongue is covered with short fur, is smooth on the edges and has been subject to soreness several times in the past two months. Two weeks after delivery free hydrochloric acid was present in the postprandial gastric juice. Two months later hydrochloric acid is not produced by alcohol stimulation but is produced by histamine injection, to which she had a severe general reaction. The red blood count is 4,700,000, the hemoglobin 104 per cent, Sahli. The spinal fluid is normal and under low pressure. The Kahn reaction is negative. She has been taking about 2.25 Gm. of dried brewer's yeast daily for six or eight weeks but no distinct improvement has occurred. She has had a small amount of liver. Phenobarbital was discontinued for a month for fear it might have been a contributing factor, but because of recurrence of epileptic siezures it has been resumed.

Theodore E. Wade, M.D., Pueblo, Colo.

ANSWER.—There is considerable clinical and experimental evidence to show that parenteral administration of either thiamine hydrochloride or liver extract is far superior to that of oral administration. The oral administration carries with it a questionable amount of absorption. In a 3,600 bed charitable hospital vitamin B_1 and liver are given parenterally. The following is suggested as an effective therapy for a case of polyneuritis of pregnancy: 3,000 units of vitamin B_1 or thiamine hydrochloride or vitamin B complex daily hypodermically for a period of from twenty-one to thirty days; a diet rich in vitamin B content such as yeast, liver, whole wheat bread, cereals, eggs, nuts, lean pork, milk, vegetables and rice polishings; nicotinic acid (vitamin B_2) in doses of 50 mg. ten times a day for three days. Vitamin therapy should be continued for at least two weeks and possibly for four before concluding that it is ineffective. From the evidence submitted in this case one should be suspicious of a subacute combined degeneration of the spinal cord related to either avitaminosis or pernicious anemia.

NO ARTERIES EXEMPT FROM ATHEROSCLEROSIS

To the Editor:—Do you know of any artery or groups of arteries in which intimal thickening, atherosclerosis or medial sclerosis never develops? In other words, are there any arteries in the body in which the lumen always remains of the same caliber and the walls remain free of destructive processes throughout life? Roy J. Popkin, M.D., Los Angeles.

ANSWER.—There is no artery which is always free from pathologic changes during a long life, although occasionally essentially normal coronary arteries are found in persons 60 years of age. Cerebral arteries are usually attacked late in life. Paradoxically the main renal arteries show less atherosclerosis than the other abdominal branches of the aorta. Lesions extending from the orifices for a short distance are common. Great hypertrophy of the media may occur with hypertension, but up to the division of the vessel there is frequently no atherosclerosis.

SOAP SUBSTITUTES FOR SENSITIVE SKIN

To the Editor:—A patient develops an allergic response to every form of soap used. Can you suggest to me some substitute for soap?

Milton H. Erickson, M.D., Eloise, Mich.

ANSWER.—Sensitivity of the skin to soap may be either nonspecific or specific. Nonspecific dermatitis is due to the lack of tolerance to the alkali content of most soaps. It is characteristic of highly irritable skin that its tolerance for alkali is low. For this reason most dermatologists forbid the use of soap (everywhere except on the scalp) in cases of eczema. Specific sensitivity to soap may be due to dyes, perfumes and other extraneous ingredients, rather than the salts of the fatty acids, which are the components of soaps. Among the ingredients to which specific sensitivity is to be considered are cottonseed oil and flaxseed oil in persons sensitive to these substances.

Soap substitutes that are frequently used are oils, as liquid petrolatum, sesame oil and various vegetable oils. Each of these should be tried in turn for the patient's tolerance to it. Another group of substances used as soap substitutes are the various sulfonated oils available commercially. Among these are Acidolate, Tersus and Drene. They have a drying effect on the skin and may require the use of a small amount of oil afterward to counteract this effect. It should be determined that the oil used is nonirritating to the individual patient.

SYPHILIS OF MOTHER, NURSING AND CONTINUED TREATMENT

To the Editor:—A woman in the fourth month of pregnancy is discovered to have positive tests for syphilis. No signs or symptoms of activity are present and the date of infection is unknown. Intensive continuous treatment was carried out to the time of delivery of a full term normal baby. The mother's tests have been persistently positive. Assuming for the sake of argument that her disease is truly latent, that her treatment was adequate by all standards and that the baby is nonsyphilitic, (1) May the mother nurse the baby? (2) May the mother have a postpartum rest period or a rest at any time during nursing? M.D., Illinois.

ANSWER.—1. The mother may nurse the baby.

2. For her own sake the mother would require more treatment than one supposes her to have had on the basis of the information supplied, and treatment therefore should be continued. If, however, she has been adequately treated for her own sake, further treatment is not necessary simply because she is nursing the baby.

POLYCYTHAEMIA VERA

To the Editor:—I am a victim of polycythaemia vera. Please inform me regarding the technic that I should use on myself with a simplex Westinghouse x-ray machine of 50 milliamperes and 85 kilowatts in treatment for this condition. If my blood count is 7,000,000, just what technic should I use. M.D., Idaho.

ANSWER.—Most internists and hematologists agree that polycythaemia vera is best treated by venesection. Irradiation may be tried. One hundred roentgens is given over the spleen three times a week for two weeks. Further irradiation must depend on the blood count.

FREQUENT MENSTRUATION AND ENLARGED THYROID IN YOUNG GIRL

To the Editor:—A girl aged 15 menstruates every two to three weeks and has a noticeable enlargement of the thyroid. She is entirely normal otherwise. In seeking authoritative opinions I have received conflicting advice. On the one hand it was suggested that she be given antuitrin-S and desiccated thyroid gland to tolerance. On the other hand I was advised that the administration of thyroid in adolescent goiter is often attended with increased thyroid activity and the frequent menstrual periods is a contraindication to any type of estrogenic therapy, the preparation of choice being corpus luteum. M.D., Wisconsin

ANSWER.—There is no connection between the enlargement of the thyroid and the frequent menstruation. The only treatment indicated in such cases is a small dose of iodine (about 10 mg. of potassium iodide a week) to prevent further enlargement of her thyroid. No attempt should be made to influence ovarian function at this age, because some spontaneous adjustment may occur soon. Moreover, the frequency of menstruation shows a considerable amount of normal variation.

TYPHUS VACCINES

To the Editor:—In Queries and Minor Notes (The Journal, Oct. 5, 1940, p. 1218) in answer to an inquiry about typhus vaccines and serums it was stated that up to the present time typhus vaccines are still in the experimental stage. Two vaccines seem to have outgrown the experimental stage and are successfully employed in routine vaccinations: 1. Weigl vaccine (Professor Weigl, director of the Polish Institute at Lodz) is considered the most effective vaccine made from the intestine of lice which have been infected with Rickettsia prowazeki. 2. The Wohlrab vaccine (Dr. Rudolf Wohlrab, author of the chapter on the typhus fever group, Handbook of Virus Diseases, 1939, vol. 2, p. 528; *Arb. Inst. exper. Therap.*, Frankfurt 38, 1939; *Ztschr. f. Hyg. u. Infektionskr.* 122: 220, 1939) does not use the classic Rickettsia prowazeki but Rickettsia mooseri, the virus of the murine typhus, and Wohlrab prefers Cox's method (chicken embryo, vitelline sac inoculation, *Pub. Health Rep.* 53: 2241 [Dec. 23] 1938). Wohlrab was making vaccine on a larger scale for the Polish campaign of the German army last fall and winter. Statistical data relating thereto could not yet be obtained. Latest reports refer to the discovery of a specific toxin, probably an endotoxin (Gildemeister and Haagen). This Rickettsia toxin is not more resistant than the virus itself and can be destroyed by formaldehyde, heating to 60 C. or storage for seven days. In mouse experiments typhus serums neutralized the specific toxin and thus prevented the occurrence of the typical exanthem as well as circulatory and nervous symptoms while they prevented incubation of infection only in single cases.

F. O. W. Voigt, M.D., Oskaloosa, Iowa.

Medical Examinations and Licensure

COMING EXAMINATIONS

NATIONAL BOARD OF MEDICAL EXAMINERS EXAMINING BOARDS IN SPECIALTIES

Examinations of the National Board of Medical Examiners and Examining Boards in Specialties were published in THE JOURNAL, November 30, page 1910.

BOARDS OF MEDICAL EXAMINERS

ALABAMA: Montgomery, June 17-19. Sec., Dr. J. N. Baker, 519 Dexter Ave., Montgomery.

ARIZONA: * Phoenix, Jan. 7. Sec., Dr. J. H. Patterson, 826 Security Bldg., Phoenix.

CALIFORNIA: *Oral examination* (required when reciprocity application is based on a state certificate or license issued ten or more years before filing application in California), Los Angeles, Dec. 11. *Written.* Los Angeles, Feb. 24-27. Sec., Dr. Charles B. Pinkham, 1020 N St., Sacramento.

COLORADO: * Denver, Jan. 7-10. Applications must be on file not later than Dec. 23. Sec., Dr. Harvey W. Snyder, 831 Republic Bldg., Denver.

DELAWARE: July 8-10. Sec., Medical Council of Delaware, Dr. Joseph S. McDaniel, 229 S. State St., Dover.

GEORGIA: Atlanta, June. Sec., State Examining Boards, Mr. R. C. Coleman, 111 State Capitol, Atlanta.

HAWAII: Honolulu, Jan. 8-11. Sec., Dr. James A. Morgan, 48 Young Building, Honolulu.

IDAHO: Boise, April 1. Dir., Bureau of Occupational License, Mr. H. B. Whittlesey, 335 State Capitol Bldg., Boise.

ILLINOIS: *Written.* Chicago, Jan. 21-22. *Reciprocity.* Chicago, Jan. 23. Supt. of Registration, Dept. of Registration and Education, Mr. Lucien A. File, Springfield.

INDIANA: Indianapolis, June 17-19. Sec., Board of Medical Registration and Examination, Dr. J. W. Bowers, Citizens Trust Bldg., Fort Wayne.

IOWA: Des Moines, Dec. 9-11. Dir., Division of Licensure and Registration, Mr. H. W. Grefe, Capitol Bldg., Des Moines.

KANSAS: Topeka, Dec. 10-11. Sec., Dr. J. F. Hassig, 905 N. Seventh St., Kansas City.

MARYLAND: *Regular.* Baltimore, Dec. 10-13. Sec., Dr. John T. O'Mara, 1215 Cathedral St., Baltimore. *Homeopathic.* Baltimore, Dec. 10-11. Sec., Dr. John A. Evans, 612 W. 40th St., Baltimore.

MICHIGAN: * Ann Arbor and Detroit, June 11-13. Sec., Board of Registration in Medicine, Dr. J. Earl McIntyre, 202-4 Hollister Bldg., Lansing.

MINNESOTA: * Minneapolis, Jan. 21-23. Sec., Dr. Julian F. Du Bois, 350 St. Peter St., St. Paul.

MISSISSIPPI: *Reciprocity.* Jackson, December. Asst. Sec., State Board of Health, Dr. R. N. Whitfield, Jackson.

MONTANA: *Reciprocity.* Helena, March 31. *Written.* Helena, April 1. Sec., Dr. S. A. Cooney, 216 Power Block, Helena.

NEVADA: *Reciprocity with oral examination,* Feb. 3. Sec., Dr. Fred M. Anderson, 215 N. Carson St., Carson City.

NEW HAMPSHIRE: Concord, March 13-14. Sec., Board of Registration in Medicine, Dr. T. P. Burroughs, State House, Concord.

NEW JERSEY: Trenton, June 17-18. Sec., Dr. Earl S. Hallinger, 28 W. State St., Trenton.

NEW MEXICO: Santa Fe, April 14-15. Sec., Dr. Le Grand Ward, 135 Sena Plaza, Santa Fe.

NEW YORK: Albany, Buffalo, New York and Syracuse, Jan. 27-30. Chief, Bureau of Professional Examinations, Mr. Herbert J. Hamilton, State Education Department, 315 Education Bldg., Albany.

NORTH CAROLINA: *Reciprocity.* Durham, Dec. 10. Sec., Dr. W. D. James, Hamlet.

NORTH DAKOTA: Grand Forks, Jan. 7-10. Sec., Dr. G. M. Williamson, 4½ S. Third St., Grand Forks.

OHIO: Columbus, Dec. 9-12. Sec., Dr. H. M. Platter, 21 W. Broad St., Columbus.

OKLAHOMA: * Oklahoma City, Dec. 11. Sec., Dr. James D. Osborn Jr., Frederick.

OREGON: * Portland, Jan. 14-16. Exec. Sec., Miss Lorienne M. Conlee, 608 Failing Bldg., Portland.

PENNSYLVANIA: Philadelphia, January 7-11. Acting Sec., Bureau of Professional Licensing, Miss Marguerite G. Steiner, 358 Education Bldg., Harrisburg.

RHODE ISLAND: * Providence, Jan. 2-3. Sec., Division of Examiners, Dr. Robert M. Lord, 366 State Office Bldg., Providence.

SOUTH DAKOTA: * Pierre, Jan. 21-22. Dir., Medical Licensure, Dr. J. F. D. Cook, Pierre.

TENNESSEE: Memphis, Dec. 18-19. Sec., Dr. H. W. Qualls, 130 Madison Ave., Memphis.

VERMONT: Burlington, Feb. 11. Sec., Dr. W. Scott Nay, Underhill.

WASHINGTON: * Seattle, Jan. 13-15. Sec., Department of Licenses, Mr. Nelson N. Vaughan, Olympia.

WISCONSIN: * Madison, Jan. 14-16. Applications must be on file not later than Jan. 2. Sec., Dr. H. W. Shutter, 425 E. Wisconsin Ave., Milwaukee.

WYOMING: Cheyenne, Feb. 3-4. Sec., Dr. M. C. Keith, Capitol Bldg., Cheyenne.

* Basic Science Certificate required.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

ARIZONA: Tucson, Dec. 17. Sec., Dr. Robert L. Nugent, University of Arizona, Science Hall, Tucson.

COLORADO: Denver, Dec. 9-10. Sec., Dr. Esther B. Starks, 1459 Ogden St., Denver.

CONNECTICUT: Feb. 8. Address State Board of Healing Arts, 1945 Yale Station, New Haven.

DISTRICT OF COLUMBIA: Washington, April 21-22. Sec., Commission on Licensure, Dr. George C. Ruhland, 203 District Bldg., Washington.

IOWA: Des Moines, Jan. 14. Dir., Division of Licensure and Registration, Mr. H. W. Grefe, Capitol Bldg., Des Moines.

MICHIGAN: Ann Arbor, Detroit and East Lansing, Feb. 14-15. Sec., Miss Flora E. Dube, East Lansing.

MINNESOTA: Minneapolis, Jan. 7-8. Sec., Dr. J. Charnley McKinley, University of Minnesota, 126 Millard Hall, Minneapolis.

NEBRASKA: Omaha, Jan. 14-15. Dir., Bureau of Examining Boards, Mrs. Clark Perkins, 1009 State Capitol Bldg., Lincoln.

OREGON: Portland, Feb. 15. Sec., State Board of Higher Education, Mr. Charles D. Byrne, University of Oregon, Eugene.

SOUTH DAKOTA: *Endorsement.* Yankton, Dec. 21. Sec., Dr. Gregg M. Evans, Yankton.

WASHINGTON: Seattle, Jan. 9-10. Sec., Department of Licenses, Mr. Nelson N. Vaughan, Olympia.

Idaho April Report

Mr. H. B. Whittlesey, director, Bureau of Occupational Licenses, reports the written examination for medical licensure held at Boise, April 2-6, 1940. The examination covered twenty-one subjects and included 140 questions. An average of 75 per cent was required to pass. Twenty-three candidates were examined, twenty-two of whom passed and one failed. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
College of Medical Evangelists		(1937)	79, 81.5
Loyola University School of Medicine		(1940)	85
Northwestern University Medical School		(1928) (1936) 79, 83, (1938) 82.5, (1939) 79, 83	81,
Rush Medical College		(1937) (1938) 82, (1939) 81.5	83.5,
University of Illinois College of Medicine		(1935)	81
University of Louisville School of Medicine		(1939)	83
University of Maryland School of Medicine and College of Physicians and Surgeons		(1925)	83,
University of Michigan Medical School		(1935)	79
Washington University School of Medicine		(1938) (1939) 81.5	83,
Creighton University School of Medicine		(1933)	83
University of Oklahoma School of Medicine		(1939)	83
University of Oregon Medical School		(1932) 81, (1939)	82.5

School	FAILED	Year Grad.	Number Failed
Regia Università degli Studi di Bologna. Facoltà di Medicina e Chirurgia		(1937)	1

Pennsylvania Reciprocity Report

Miss Marguerite G. Steiner, acting secretary, Bureau of Professional Licensing, reports thirty-three physicians licensed to practice medicine by reciprocity and twenty-one physicians so licensed by endorsement from January 26 through September 18. The following schools were represented:

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
University of Colorado School of Medicine		(1931)	Colorado
Yale University School of Medicine		(1932)	Connecticut
Loyola University School of Medicine		(1938)	Illinois
Rush Medical College		(1931), (1937) (1934) Michigan	Illinois,
State University of Iowa College of Medicine		(1935)	Iowa
Johns Hopkins University School of Medicine		(1933), (1937)	Maryland
University of Maryland School of Medicine and College of Physicians and Surgeons		(1936)	Maryland
Harvard Medical School		(1939)	Maryland
University of Michigan Medical School		(1929)	Michigan
Wayne University College of Medicine		(1940)	Michigan
University of Minnesota Medical School		(1936)	Minnesota
St. Louis University School of Medicine		(1935)	Florida
University of Nebraska College of Medicine		(1933)	Nebraska
Columbia University College of Physicians and Surgeons		(1932), (1934, 2)	New York
Cornell University Medical College		(1924)	New York
Long Island College of Medicine		(1935)	New York
University of Buffalo School of Medicine		(1932)	New York
Ohio State University College of Medicine		(1933)	Ohio
University of Cincinnati College of Medicine		(1927)	Ohio
Hahnemann Medical College and Hospital of Philadelphia		(1934), (1935)	New Jersey
Jefferson Medical College of Philadelphia		(1929) (1935) West Virginia	Texas,
Temple University School of Medicine		(1937)	Kentucky
University of Pennsylvania School of Medicine		(1928), (1934) New Jersey	
Meharry Medical College		(1937)	Tennessee
University of Tennessee College of Medicine		(1930)	Tennessee

School	LICENSED BY ENDORSEMENT	Year Grad.	Endorsement of
Georgetown University School of Medicine		(1938)	N. B. M. Ex.
Northwestern University Medical School		(1938), (1939)	N. B. M. Ex.
Johns Hopkins University School of Medicine		(1938), (1939) N. B. M. Ex.	
Boston University School of Medicine		(1938, 2)	N. B. M. Ex.
Harvard Medical School		(1925), (1932), (1934), 1936), (1937) N. B. M. Ex.	
Washington University School of Medicine		(1934)	N. B. M. Ex.
Columbia University College of Physicians and Surgeons		(1932)	N. B. M. Ex.
Syracuse University College of Medicine		(1938)	N. B. M. Ex.
Duke University School of Medicine		(1937, 2), (1939) N. B. M. Ex.	
University of Cincinnati College of Medicine		(1929)	N. B. M. Ex.
University of Pennsylvania School of Medicine		(1935)	N. B. M. Ex.
Woman's Medical College of Pennsylvania		(1938)	N. B. M. Ex.

Book Notices

The Emperor's Itch: The Legend Concerning Napoleon's Affliction with Scabies. By Reuben Friedman, M.D., Assistant Professor of Dermatology and Syphilology, Temple University School of Medicine, Philadelphia. Cloth. Price, $1.50. Pp. 82, with 10 illustrations. New York: Froben Press, 1940.

It is said that 40,000 books have been written on the life of Napoleon, but the present interesting monograph by Friedman is the first which discusses an annoying disease of the skin from which he suffered for many years. This phase of Napoleon's life has either been overlooked or been misunderstood by previous biographers.

The story that the disease of the skin from which Napoleon suffered was scabies is shown by the author to be a myth. There are no authentic records to prove that he ever had this disease. In view of the emperor's cleanly habits and the long duration of the disorder and because of the numerous sulfur baths which he took, it seems impossible that the disease could have been scabies. Furthermore, the Empress Josephine is not known to have suffered from scabies, although Napoleon's second wife, Marie Louise, is said to have been affected. However, it has been stated that she was somewhat promiscuous sexually. Finally, the remedy which his physician Corvisart used successfully was an extremely weak and practically useless one for the treatment of scabies.

The author suggests with good reason that Napoleon actually suffered from dermatitis herpetiformis, which began with the siege of Toulon and lasted for nine or ten years. The temporary "cure" effected by his physician coincided with the period of his life when he was able to rest and be relieved of the strain of his military campaigns. The author also thinks that Napoleon's characteristic pose with his hand beneath his shirt was a mannerism possibly cultivated in his boyhood. He does not think it was due to itching from his cutaneous disease.

This book is a most readable one and contains many references and interesting illustrations.

An Introduction to Medical Genetics. By J. A. Fraser Roberts, M.A., M.B., D.Sc., Principal Investigator to the Burden Mental Research Trust, Stoke Park Colony, Stapleton, Bristol. Cloth. Price, $4.50. Pp. 266, with 94 illustrations. New York & London: Oxford University Press, 1940.

Works on human heredity have not heretofore been distinguished by any evident relevance for clinical medicine. In Dr. Roberts's volume, perhaps for the first time, the relation of genetics to medical practice, and especially to medical research, can be seen clearly. The author, moreover, by a somewhat novel method of presenting genetic principles has achieved a clarity and simplicity which are exceptional, in comparison not only with other textbooks but even with avowed popularizations of the subject.

There is no conventional prefatory section on genetic principles. Instead there is a discussion in turn of each type of mating which may be encountered in man: normal by abnormal, abnormal by abnormal and normal by normal, for conditions which exhibit respectively dominant, recessive or incompletely dominant inheritance, and autosomal or sex linked transmission. The discussion of each case is in terms of a familiar human abnormality and is followed by a clear explanation of the chromosomal basis for the observed results. Genetic principles, developed gradually in the course of the book, are limited strictly to those which are immediately applicable to human material. Special statistical methods, necessary for the actual analysis of human hereditary mechanisms but not essential for an understanding of them, are not elaborated, but the precautions which must be observed in the collection and interpretation of data in order to avoid the commoner statistical fallacies are carefully pointed out. Even so difficult a subject as the detection of human linkage is not ignored, and once again the author explodes the still current notion that the association of two abnormal traits indicates that they are linked in the genetic sense.

Topics of subsidiary importance or of especial technical complexity are relegated to fine type and may be omitted by the reader without sacrificing the continuity or coherence of the remainder of the text. But in spite of the modest dimensions of the book it is doubtful whether any single principle essential for the understanding of human genetic methods fails to receive at least passing attention, with judicious orientation into what is already an unwieldy literature for the uninitiated.

There are inevitably some sections with which it would be tempting to take issue. Thus Roberts seems overoptimistic with regard to the prognostic possibilities promised by the prospect of constructing linkage maps for man. It is quite true, of course, that the accumulation of cases of genetic linkage is almost bound to follow any systematic effort to discover them. But it is a far cry from the discovery of isolated cases of linkage to the development of usable gene maps such as have been elaborated so brilliantly for Drosophila and maize. Even in the mouse, in which the difficulty inherent in a larger number of chromosomes is roughly of the same magnitude as in man, chromosome maps are still a dream for the future in spite of this animal's convenience for laboratory experiments and the extensive genetic investigations of which it has been the subject. This is not to deny the value of linkage studies in man but it does suggest the importance of pursuing human genetic studies as human genetics and of recognizing at the outset the conditions (not all unfavorable, as is frequently supposed) which establish the methodology of human heredity on a somewhat different level from that of the genetics of laboratory bred animals.

It is the special merit of the book that it reveals the conditions by which human genetics, especially in its medical aspects, is qualitatively distinguished from the conventional genetics of the animal or plant breeder. And it is important to recognize that the classic materials presented in standard biologic textbooks may give a misleading or totally false picture of what is to be expected in human material. The excellent sections on the similar effects of different genes, on the variable expression of heredity factors and on heredity as a factor in the causation of disease, together with constant emphasis on the peculiar significance of gene frequency in man, succeed in establishing the proper orientation. One gets the impression that the part played by heredity in a large majority of pathologic conditions is to determine the presence or absence of a constitutional peculiarity which might be called a diathesis, although it involves a more tangibly determinable condition than that term usually connotes. From the evidence available it seems almost certain that this situation is far commoner than is any unequivocal one to one correspondence between gene and disease. Genetic study can assist the clinician by making possible the detection of diathetic individuals even when they do not develop the disease, and this should facilitate the detection of such controllable nongenetic factors as infection, diet and mechanical irritation, which may play a part in transforming an inherited diathesis into a patent pathologic condition.

The reader should be warned that Dr. Roberts's theoretical discussions of the various ways in which genetic factors may be concerned in the development of disease have the appearance of being rather more speculative than need be. This is partly to be attributed to a commendably conservative approach but chiefly, perhaps, to the author's limiting himself exclusively to human heredity in his choice of illustrative material. In this connection primarily the disadvantages of this restriction are seen, for a judicious selection of well established analogues from animal genetics would have furnished a firmer basis for many of the inferences which appear rather tenuous when supported only by observations from the less adequately studied human material. For example, the author suggests that certain genes may act by rendering the developing embryo especially sensitive to environmental variations which are without effect on genetically normal organisms; the suggestion would appear less gratuitous if it were indicated that this type of action has frequently been demonstrated for genetic factors studied in laboratory animals. And the whole field of what is commonly called developmental or physiological genetics has such an intimate bearing on the specifically medical problems of human heredity that some familiarity with its methods and results would seem to be an indispensable part of the medical geneticist's background.

The defects which may be found in this volume are minor in comparison with the values inherent in its fresh outlook and in its temperate treatment of most problems. Of specific sections, the chapter on multifactor inheritance is perhaps the least satisfactory, and it would probably have been better to omit entirely a consideration of hereditary factors in intelligence if it was not possible to give somewhat more extensive indication of the complexities of the problem. The practical minded reader may be disturbed by the fact that many of the illustrations of clearcut mendelizing pathologic conditions are still such rare or insignificant aberrations as albinism, alkaptonuria or polydactyly. But an understanding of the book will involve recognition that this is largely a consequence of the inadequacy of traditional methods in human genetic research and an appreciation of the fact that the importance of genetics for medicine considerably transcends its relevance to such conditions as those just enumerated. The use of genetic methods as a tool to supplement the usual methods of clinical research is more than likely to shed light on the etiology and pathogenesis of leukemia, gastric ulcer and essential hypertension, for example, and to prove profitable in the further study of such infectious diseases as rheumatic fever and poliomyelitis, to name only a few of the conditions in which there is already some basis for inferring the importance of hereditary factors.

Medical practitioners and investigators will find the book a comprehensible and stimulating guide to the applicability of genetics to medicine. It can also be recommended to specialists in animal or plant genetics who wish a clearer idea of some of the human applications of their subject. And it should prove an admirable textbook either for a semester's course in the premedical curriculum or as the basis for a brief lecture series in genetics for medical students.

Expectant Motherhood. By Nicholson J. Eastman, M.D., Professor of Obstetrics in Johns Hopkins University, Baltimore. Cloth. Price, $1.25. Pp. 176, with 9 illustrations. Boston: Little, Brown & Company, 1940.

This is another of the numerous books which have appeared during the last few years attempting to educate expectant mothers about pregnancy and labor. Not only has the author admirably succeeded in presenting this information in simple language, but throughout the book he allays possible fears and explains away absurd ideas and superstitions connected with childbirth. Every woman who reads this or a similar book will find out what occurs to her and her baby during pregnancy and labor. Furthermore, it will make her realize the great value of good antepartum care and the importance of selecting a good physician and a satisfactory hospital for her confinement. This book should be recommended to women who plan to have a baby.

Preventive Medicine. By Mark F. Boyd, M.D., M.S., C.P.H., Field Staff Member, International Health Division of the Rockefeller Foundation. Sixth edition. Cloth. Price, $5. Pp. 588, with 168 illustrations. Philadelphia & London: W. B. Saunders Company, 1940.

The publication of the sixth edition of this standard textbook of preventive medicine is evidence both of the esteem in which it is held and the rapid progress of development in the field of public health. Its greatest usefulness is as a textbook in courses on preventive medicine in medical schools and universities and as a guide to physicians whose public health activities are largely incidental to clinical practice. The book has recognized standing.

The Early Diagnosis of the Acute Abdomen. By Zachary Cope, B.A., M.D., M.S., Surgeon to St. Mary's Hospital, Paddington. Eighth edition. Cloth. Price, $3.75. Pp. 257, with 36 illustrations. New York & London: Oxford University Press, 1940.

This edition of Cope's famous monograph embodies few additions. Little can be said in further praise of this small but justly popular book that has not already been said in past reviews. A compact volume, it treats with utmost clarity the entire subject of acute conditions of the abdomen. Particularly excellent are the chapters on the method of examining the abdomen and the opening chapter on the principles of diagnosis. The importance of a detailed history is emphasized. Charts illustrating the reference of pain and manual methods of examination are distinctly helpful. Anatomic considerations are utilized to explain the basis for the various diagnostic procedures. Well known to most, it should be pointed out that this volume has a place on the shelf of every student, surgeon and physician whose work may be even remotely related to pathologic conditions of the abdomen.

The Unseen Plague—Chronic Disease. By Ernst P. Boas, M.D., Chairman, Committee on Chronic Illness Welfare Council of New York City. Cloth. Price, $2. Pp. 121, with 2 illustrations. New York: J. J. Augustin, Publisher, 1940.

As an administrator of a hospital a large part of which is devoted to the care of the chronically afflicted, as a clinician and as chairman of a permanent committee on chronic illness of the Welfare Council of New York City the author has had ample opportunity to study the various phases of the problem with which he deals. With the exception of mental diseases, tuberculosis and to a certain extent cancer, adequate provision has not been made anywhere for the care of the legions of sufferers from the diverse disabling and crippling illnesses. The book deals comprehensively and conscientiously with the medical, social and organizational aspects of the situation; it takes a discouraging view of the preventive possibilities which lie mainly in popular education and in clinical and laboratory studies on the causes and methods of treatment of the degenerative diseases. According to the author, only improved socioeconomic conditions can bring about a real remedy. He develops this point of view in the chapter on public responsibility for the chronic sick, on page 47 of which he says rather impetuously:

> An aroused community, in self preservation as well as for humanitarian reasons, must face the fact that the bare existence forced on so large a proportion of our population generates and accelerates disease and undermines the health of vast numbers of citizens. Steady employment, fair wages and proper housing will prevent more disease than most laboratory research and educational ballyhoo about disease prevention.

Neither such occasional outbursts as the one quoted nor the few minor statistical inaccuracies and some inconsistencies of statement detract from the value of the book and the serious challenge it presents to the medical profession and to every thinking man and woman. The best written chapter is that on the aged, and the one dealing with the community program for the care of the chronic sick is the most constructive. The book is provocative of thought and may stimulate not only interest in the problem but action to deal with it in a way its gravity demands.

Psychology and Psychotherapy. By William Brown, D.M., D.Sc., F.R.C.P., Hon. Consulting Psychologist, Bethlem Royal Hospital, Beckenham, Kent. Fourth edition. Cloth. Price, $4.75. Pp. 260. Baltimore: William Wood & Company, 1940.

The publication of a fourth edition of this little book is ample evidence of its reception and appraisal. The contents frankly and unequivocally deal with psychiatry from a psychoanalytic point of view. Nevertheless, the contributions of all the great schools of psychology are considered and utilized when applicable. This is an excellent introductory book for students of psychiatry.

The Sexual Perversions and Abnormalities. By Clifford Allen, M.D., M.R.C.P., D.P.M., Physician in Charge of the Psychiatric Department of the Seamen's Hospital, Greenwich. Cloth. Price, $2.25. Pp. 193. New York & London: Oxford University Press, 1940.

The author has with great courage attempted to consider the sexual perversions with a view to indicating the possibilities of therapy for them. His clinical material indicates a wide experience and his therapeutic results by a diversity of methods seem to have been gratifying. The possibilities of cure or amelioration of perversions without lengthy psychoanalysis are convincingly presented by the author from his own material.

La fotografía de las membranas profundas del ojo. Por Manuel de Rivas Cherif. Paper. Pp. 75, with 52 illustrations. Mexico: La Casa de España en México, 1940.

In this booklet there is a brief review of the history and optics of some of the more important cameras used in photographing the fundus of the eye. The pamphlet is well printed on good paper. The diagrams of the cameras and the optical aspects are not bad but the pictures of the fundi are so hopeless that they seem to have been developed under the influence of Rivera. The two color plates are worst of all, the fundus being depicted as a sickish pink-brown.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Workmen's Compensation Acts: Reactivated Tuberculosis an Occupational Disease.—The employee in this case had pulmonary tuberculosis which had been in an inactive stage for some sixteen years. He was employed as a grain scooper, which work required him to go into the holds of grain ships and there to operate steam shovels by which the grain was brought within the reach of moving buckets. In the holds of such ships the air was impregnated with minute particles of husk, mustard-seed and dirt. Some time about the middle of the year of 1934 the employee began to have difficulty with his breathing, and his dormant tuberculous condition became reactivated. By June 15, 1936, he became totally disabled and filed a claim for compensation under the longshoremen's and harbor workers' compensation act. The commissioner awarded compensation, the United States district court for the western district of New York affirmed that award and the employer appealed to the United States circuit court of appeals, second circuit.

There was sufficient testimony, in the opinion of the court, to justify the conclusion that hard manual work done for long periods in dust-laden atmosphere tends to produce fibrosis of the lungs, which in turn weakens resistance to any latent tuberculous infection and reactivates that infection. This is what happened in the present case. The important question before the court was whether or not the disability was an injury arising out of employment. If so, it was either an "accidental injury" or an "occupational disease." The court agreed with the commissioner making the award in the first instance that it was an occupational disease. The court was of the opinion that the compensation act should not be extended so as to make it a general health insurance and that to avoid this the coverage must be limited to diseases resulting from working conditions peculiar to the calling. In order to recover a workman must, the court continued, be exposed to hazards greater than those involved in ordinary living, and the disease must arise from one of these hazards. But, although it must be found that special dangers exist in the employment and that the disease arises from such dangers, the court could see no reason for limiting the protected class to those who have a normal resistance to such diseases or for excluding those who are abnormally vulnerable. It might be desirable that the second group should not be employed under such conditions at all, but members of that group may not be charged with ignorance, carelessness or acceptance of the risk because they are. Such considerations, the court pointed out, are alien to the underlying theory of workmen's compensation, which makes industrial disabilities, so far as they are truly attributable to the industry, a part of the cost of production and throws compensation for them on the consumer. This is not because the consumer is at fault for creating the demand whose supply produces the disabilities but because a loss shared among many is less a loss than if borne by one. Since all who actually work in the industry are necessary to the supply, the injuries of all, whether or not they are normally resistant to the unwholesome conditions pervading it, are part of the cost of producing that supply, and compensation for them is within the scheme. It would be an especially harsh interpretation which would exclude just those who are most in need of protection.

The court could see no difference between an acute infection and the awakening of an old one. The compensation act is not concerned with pathologic conditions but with industrial disability; a disease is no disease until it manifests itself. Few adults, the court said, are not diseased, if by that is meant only that the seeds of future troubles are not already planted, and it is commonplace that health is a constant warfare between the body and its enemies. An infection mastered, though latent, is no longer a disease, industrially speaking, until the person's resistance is again so far lowered that he succumbs. It was contended that so broad a construction of the compensation act would result in premiums going to prohibitive heights or that all persons who enter a calling must be examined and the weaker ones excluded. It is possible, the court answered, that the added cost of the system will so raise prices as to throw some workmen out of employment, but so far as it is true one must choose between cheaper and larger production, carried on with less regard for the producers, and a restricted output made under better conditions. Whatever the proper path, the court concluded, it was not for the courts to plot it, and it was enough that the award in the present case seemed to the court to carry out the scheme of the compensation act and fall fairly within the language chosen to embody it. The award in favor of the employee was therefore affirmed.—*Grain Handling Co., Inc., v. Sweeney, 102 F. (2d) 464.*

Malpractice: Death of 6 Year Old Boy Attributed to Chiropractic Adjustments.—Contending that the death of her 6 year old son was due to the carelessness and negligence of the defendant chiropractor, the plaintiff brought suit and obtained a judgment for $10,000. The defendant then appealed to the district court of appeal of California.

The plaintiff, according to her testimony, first noticed that her son was "stooping a bit." He complained that it had been painful for him to stand erect since a boy bumped him at school. Later a weakness of the legs developed and the plaintiff and her husband took the child to the defendant chiropractor. After roentgenograms had been taken the defendant, according to the plaintiff's testimony, attributed the boy's condition to a misplacement of a vertebra. He then proceeded to give an "adjustment" and continued this form of treatment about every three days for nearly four months, until the boy died. After four or five adjustments the boy developed a temperature of about 100 F. During the course of treatment he lost vitality, weight and color, he complained of pain when the adjustments were being given, and "paralysis was coming from the legs to the arms, and he was completely paralyzed."

From time to time the plaintiff had conversations with the defendant with respect to the child's condition, and the defendant assured her that it was not necessary to call in a doctor because "the only thing the boy had was a certain pressure on the spinal cord, on account of the misplaced vertebra, and he was doing the best thing, and nothing more could be done for the child." The defendant was called as a witness by the plaintiff and he testified that he took roentgenograms of the boy's spine and found "a subluxation of the second cervical vertebra, impinging the nerves, and causing a congestion in the cord," as well as a "rotation of the second, third and fourth cervical." He admitted that he had made no laboratory tests, urinalysis, blood count or other test except the roentgen study and an examination of the spine with his hands, and he found no abnormality, swelling, tumor, contusion or abrasion other than the condition of the second cervical vertebra. He then testified, in part, as follows:

Q.—Did you make any diagnosis of his condition at that time? *A.*—In chiropractic, we don't use the term "diagnosis." I take it that you want to know if I placed a name on his condition?

Q.—Yes. I want to know if you came to a conclusion? *A.*—Yes, I came to a conclusion, but in chiropractic we term it "analysis" instead of "diagnosis." . . . My analysis was that he had a subluxation of the second cervical vertebra, causing an impingement of the nerves at that point. . . .

Q.—Well, was that an impingement of the nerves or of the cord? *A.*—Well, it might have been from both. It was apparent from his condition that there was inflammation of the cord. The inflammation might have been from pressure on the spinal nerves, or upon the cord itself. . . .

Q.—So, it was your finding and your conclusion that at all times, from the time of your first treatment to the last, there was some inflammation and congestion of the spinal cord at the region of the cervical vertebrae? *A.*—Yes.

A physician associated with the office of the county coroner testified that an autopsy which he performed on the body of the boy "showed the body thin, the lungs congested, the left lung being pneumonic, and both lungs studded with small

tubercles. The heart, liver and stomach were normal. . . . There was no evidence of spinal or other injury. . . . I had been informed that there was some spinal condition existing, and I therefore examined the spine to see if I could find any abnormality, which I did not find." He further testified that in his opinion the boy during the early stage of his illness had tuberculosis of the meninges of the brain, or coverings of the brain. "At that time," this witness testified, "he showed paralysis, which is a typical symptom of early meningitis." In reply to a question as to what effect a chiropractic adjustment of the second cervical vertebra would have when tuberculosis of the spine exists he replied: "It would be detrimental, as rest and quiet would be absolutely indicated in those cases" and that the adjustment would accelerate or increase the existing inflammation. Another doctor of medicine testified that the boy had "some form of meningitic irritation, probably tuberculous in character," and that he was probably suffering from a secondary tuberculosis of the spine. All these witnesses agreed that the chiropractic adjustments were contraindicated and that if the boy had received proper medical attention his chances of recovery would have been good. "I would say that the child died because of lack of proper medical attention, sanitary care and proper fixation," one of the witnesses testified.

In the opinion of the district court of appeal, there was substantial evidence in the record from which the jury could infer that the course of treatment persisted in by the defendant was not of that degree of care, diligence and skill possessed and used by prudent, skilful and careful practitioners of medicine practicing in the same vicinity. The court disagreed with the defendant's contention that the testimony of the doctors of medicine called by the plaintiff should have been excluded because they were not chiropractors. In so holding, the court quoted from *Hutter* v. *Hommel,* 213 Cal. 677, 3 P. (2d) 554:

> We might add that we are cited to no rule obtaining in this jurisdiction and know of none which would preclude a physician trained in one medical school from testifying in a proper case as to the treatment rendered by a physician or surgeon trained in a different school. Such a rule might be promulgated where charges of negligence in a malpractice case are directed toward some special course of treatment to be tested by the general doctrine of a particular school, but it is not applicable to a case of this character where the alleged malpractice is based upon general charges of negligence relating largely to matters of almost common observation within the experience of every physician and surgeon.

The court could find no error in the record and therefore affirmed the judgment for the plaintiff.—*Abos v. Martyn (Calif.), 88 P. (2d) 797.*

Malpractice: Liability of Physician and Municipality to Patient in Municipal Institution.—A New York statute (Consol. Laws, ch. 24, section 50-d) imposes on a municipality ultimate liability for personal injuries sustained by reason of the malpractice of a physician or dentist while rendering services gratuitously to any person in a public institution maintained in whole or in part by the municipality. In the judgment of the Court of Appeals of New York, this statute creates a new remedy against the municipality in favor of the injured person. A physician or dentist who renders services to patients in such an institution and is negligent may still be sued on his common law liability for malpractice, but he has the right to insist that in accordance with the statute he be saved harmless by the municipality. The effect of any action, whether brought against the municipality or the physician or dentist, is determined by the provisions of the statute, and such action may be maintained only if the provisions of the statute relating to commencement of action and filing of notice of intention to commence action against the municipality are complied with strictly. Accordingly, the court held that the trial court had not erred in granting the motion of the defendants, a physician and others charged with malpractice incident to rendering services to a patient in a municipal institution, that the complaint be dismissed because the plaintiffs had failed to comply with the provisions of the statute pertaining to commencement of action and the giving of notice to the municipality of institution of suit. Judgment for the defendants was therefore affirmed.—*Derlicka et al. v. Leo et al. (N. Y.), 22 N. E. (2d) 367.*

Society Proceedings

COMING MEETINGS

American Association for the Study of Neoplastic Diseases, Baltimore, Dec. 19-21. Dr. Eugene R. Whitmore, 2139 Wyoming Ave. N.W., Washington, D. C., Secretary.
American Society of Anesthetists, New York, Dec. 12. Dr. Paul M. Wood, 745 Fifth Ave., New York, Secretary.
American Student Health Association, Ann Arbor, Mich., Dec. 27-28. Dr. Ralph I. Canuteson, University of Kansas, Lawrence, Kan., Secretary.
Annual Congress on Industrial Health, Chicago, Jan. 13-15. Dr. Carl M. Peterson, 535 N. Dearborn St., Chicago, Secretary.
Eastern Section, American Laryngological, Rhinological and Otological Society, Philadelphia, Jan. 10. Dr. N. S. Weinberger, Robert Packer Hospital, Sayre, Pa., Chairman.
Middle Section, American Laryngological, Rhinological and Otological Society, Chicago, Jan. 27. Dr. Walter H. Theobald, 307 North Michigan Blvd., Chicago, Chairman.
Puerto Rico, Medical Association of, San Juan, Dec. 13-15. Dr. David E. Garcia, P. O. Box 3866, Santurce, Secretary.
Society of American Bacteriologists, St. Louis, Dec. 27-29. Dr. I. L. Baldwin, Agricultural Hall, University of Wisconsin, Madison, Wis., Secretary.
Southern Section, American Laryngological, Rhinological and Otological Society, Nashville, Tenn., Jan. 8. Dr. William G. Kennon, Doctors Bldg., Nashville, Tenn., Chairman.
Southern Surgical Association, Hot Springs, Va., Dec. 10-12. Dr. E. Alton Ochsner, 1430 Tulane Ave., New Orleans, Secretary.
Texas Ophthalmological and Oto-Laryngological Society, Fort Worth, Dec. 13-14. Dr. Dan Brannin, Medical Arts Bldg., Dallas, Secretary.
Western Section, American Laryngological, Rhinological and Otological Society, San Francisco, Feb. 1-2. Dr. Robert C. Martin, 384 Post St., San Francisco, Chairman.

THE AMERICAN RHEUMATISM ASSOCIATION

Seventh Annual Meeting, held in New York, June 10, 1940

DR. LORING T. SWAIM, Boston, Secretary

Mono-Articular and Pauciarticular Arthritis in Children

DR. WILLIAM T. GREEN, Boston: This report concerns a study of children with mono-articular arthritis involving the knee, and pauciarticular (paucitas, Latin, a small number) arthritis in which more than one and not exceeding four joints were involved. In all, forty-three instances of arthritis of the knee and thirty-five of pauciarthritis were studied.

The results to date may be thus summarized: In the Boston area arthritis of mono-articular and pauciarticular type in children is more commonly nonspecific than due to syphilis or tuberculosis. In the pauciarticular and, to a lesser extent, in the mono-articular series, instances in which the symptoms and signs in the joints did not persist over two weeks were frequently found by later determinations to have been due to rheumatic fever. In both groups, when the symptoms and signs persisted over two weeks, they were likely to be prolonged with an average duration of $1\frac{3}{12}$ years. In many of the cases of longer duration the relationship to atrophic arthritis was suggested because the joint manifestations in a large number of the patients were similar to those seen in generalized atrophic arthritis and because three patients in the pauciarticular and one in the mono-articular groups developed generalized atrophic arthritis after a quiescent period of several years. Lengthening of the involved extremity was a common feature in both groups. In twelve of the cases in which the knee was involved there was an average lengthening of 1.3 cm. with squaring of the epiphyses. The treatment, in mono-articular and pauciarticular arthritis of long duration, should be that used in atrophic arthritis. Traction is ideal to correct deformity and develop motion.

DISCUSSION

DR. J. ALBERT KEY, St. Louis: Long ago I heard Dr. Osgood say "When confronted with chronic progressive mono-articular arthritis in a child, the diagnosis is tuberculosis until proved otherwise." I still believe that statement. I do not know what toxic arthritis is. These cases impress me as infectious. Some of them may turn out to be rheumatic fever. Some of them may be true Still's disease. Surgery might be of value if one was assured that they would become chronic. Synovectomy might be definitely indicated. Synovectomy would prevent deformity; it might prevent recurrence, and it might cure the disease. What other treatment besides high vitamin diet does Dr. Green advocate and on what basis was a low carbohydrate diet given?

DR. WALTER BAUER, Boston: Arthritis confined to one or two joints in children is all too frequently called toxic arthritis, a vague, meaningless diagnostic label. Evidently the situation in children is not unlike that in adults, namely that a certain percentage of patients with a mono-articular or "pauciarticular" arthritis are suffering from an atypical form of rheumatic fever or rheumatoid arthritis. What the others represent can be told only by the passage of time and further follow-up studies. It is important to appreciate that joint involvement in rheumatoid arthritis is not always symmetrical, particularly at the onset. Thirty per cent of our patients were atypical in this respect. Until our knowledge of joint diseases is greatly enhanced, the use of the term toxic arthritis is equivalent to saying we do not know. Such being the case, is it not preferable that we label them diagnosis unknown and hope that continuous follow-up study will give us the correct answer in many instances?

DR. M. H. DAWSON, New York: Were antistreptolysin titers determined on these patients? Some of the cases in this group which eventually clear up without residual joint changes are possibly atypical manifestations of rheumatic fever.

DR. WILLIAM T. GREEN, Boston: The antistreptolysin titers have not been determined. I treat this type of arthritis of longer duration exactly as atrophic arthritis. The same problem is involved. In those of briefer duration, the same preliminary treatment should be adopted as that for rheumatic fever. The local treatment in the chronic group involves the active correction of the deformity. Traction applied to the joints allows correction of the deformity and active painless motion. Perhaps one of the reasons why joints do better under such a regimen is that motion stimulates absorption from the joints, as has been shown by Bauer and others. There is no definite justification for any dietary regimen in arthritis, yet in the majority of instances I have recommended a low carbohydrate and high vitamin diet. The general health of these children must be promoted in all possible ways. The best "medicine" is rest.

Heberden's Nodes: Heredity in Hypertrophic Arthritis of the Finger Joints

DR. ROBERT M. STECHER, Cleveland: The present study, confined to idiopathic nodes in white women, is an analysis of the families of sixty-four individuals with Heberden's nodes. All index cases were examined personally. Information about relatives was obtained by examination when possible, otherwise by correspondence or through the family history. Fathers and brothers are not included. Of sixty-two mothers of women with Heberden's nodes, twenty were said to be affected compared to 10.3 which would be found in the general population of a group of the same size and age distribution. In 117 sisters of affected people thirty were found to be affected, compared to 10.3 which would be the expectancy in the population in general. Among 109 sisters of unaffected people in a control series the condition occurred five times compared to an expectancy of 6.26. Various family combinations were noted. Of sixty-two families the mothers were involved twenty times. Three generations of women in direct descent were found in three families. Twelve families had more than one daughter affected. In only twenty-seven of the sixty-four families studied was no evidence of familial involvement discovered. In three families with multiple involvement the probability of such combinations occurring in the same family by chance alone were found to be 1 in 190, 1 in 4,500,000 and 1 in 10,000,000 families. As Heberden's nodes is essentially a disease of later life, it seems unlikely that a common environmental factor was responsible for the condition in several members of the same family. The condition found among families of patients with Heberden's nodes is best explained by a strong hereditary influence.

DISCUSSION

DR. MORTON D. SCHWEITZER, New York: There is a substantially higher incidence among the sisters and mothers of the index cases than in the control series. I should reckon the probabilities in the three pedigrees differently. The total probability in a family is the sum of the probabilities of each member. By this method the results would also appear significant, although smaller than Dr. Stecher finds. I regard this as suggestive of a possible hereditary basis, but not proved, since the other factors suggested by Dr. Stecher as possibly operating in this condition might also occur more frequently in the family group. There are several technics appropriate for this type of study. A "gene frequency" analysis is particularly useful in the study of conditions which occur as frequently in the population as do Heberden's nodes. Since it is difficult to get all members of the family into the clinic for study, mother-daughter correlations might prove of value. Dr. Stecher, is there any possible relationship between traumatic and idiopathic nodes to be considered and may there be common susceptibility factors underlying the two types? With regard to the sex, the principal difference in the tables is a delayed onset in males of about ten years, in comparison with females.

DR. HOMER F. SWIFT, New York: Has Dr. Stecher analyzed the susceptibility of these patients to trauma? Are their hands specially exposed to injury? From the hereditary standpoint were the siblings compared with the patients in reference to exposure to functional trauma? This factor would be different in a man working in an office and using a pencil and in a scrub woman or a stone mason. In several cases recently observed one or two finger joints specially subjected to functional trauma developed arthritis while the less vigorously used joints remained normal.

DR. J. ALBERT KEY, St. Louis: There is a strong hereditary factor in hypertrophic arthritis. Trauma may produce it experimentally, but clinically there are a great many cases in which it is not produced by trauma. Heberden's nodes are seen in old ladies who have done no manual work in their lives.

DR. RUSSELL L. CECIL, New York: Both my father and my mother developed Heberden's nodes in the fifties. I have no Heberden's nodes. I have tried to explain this in various ways. My father was raised on a farm and, as a young man, used his hands a great deal; then he became a clergyman and used his hands but little. My mother was energetic, always sewing or darning, and used her hands a great deal. The only hard use I ever put my hands to is playing golf. My feeling is that the reason I have not developed Heberden's nodes is that I have not used my hands. I think the condition is largely the result of trauma.

DR. CURRIER MCEWEN, New York: It has been said that if trauma does play a role we should see Heberden's nodes especially in stenographers who reach the age at which osteoarthritis is common. I have not been struck by any undue occurrence of Heberden's nodes in people who used their hands in laborious work in their earlier days. This raises in my mind the question just what part trauma plays in Heberden's nodes. Three of my patients have Heberden's nodes on one hand and not on the other. In the hand in which they do not occur there had been peripheral nerve injuries with quite obvious trophic changes in the skin. In one of these patients three fingers are useful and two are paralyzed on the injured hand. There are marked Heberden's nodes on the good hand and moderate ones on the usable fingers of the injured hand, but no sign of them on the paralyzed fingers. I wonder if that speaks for the traumatic theory, since these fingers cannot be used and hence are spared trauma, or whether some trophic change prevents the formation of the nodes on those fingers.

DR. HOMER F. SWIFT, New York: In studying the influence of trauma on the causation of disease one is liable to emphasize that inflicted by external or physical forces and to neglect that arising from internal or functional factors. Drs. Smadel, Farr and I have studied this question in the induction of chronic nephritis in rats and have found that hereditary and functional traumatic factors are both important and cooperative. Acute nephrotoxic nephritis was induced in rats; when the work the kidneys performed was reduced to a low level the nephritis disappeared. When, on the other hand, the diet contained sufficient protein to maintain a normal rat in health, i. e. 18 per cent nitrogen, and the kidneys were forced to excrete that amount, one strain of rats developed severe chronic progressive nephritis. In two other strains this tendency was less marked, and chronic kidney disease was best induced by an abnormally high protein diet. In stating my original question, therefore, I did not wish to neglect the influence of heredity in the induction of arthritis but to emphasize the contributory influence of functional trauma. A full analysis of etiology would doubtless embrace both factors

as well as others, and only by keeping alert to all possibilities will one determine the ultimate answer.

DR. DAVID H. KLING, Los Angeles: Would Dr. Stecher clarify the definition of Heberden's nodes? Does he classify spur formations visualized by x-ray examination as Heberden's nodes as well as new bone formation seen in hypertrophic arthritis or does he designate any kind of swelling of the phalanges as Heberden's nodes? I have seen periarticular cystic lesions containing a gelatinous fluid that persist for years with no evidence of bony spur formation. Perhaps in these cases trauma may provoke cystic lesions, owing to degeneration of the soft periarticular tissues.

DR. PHILIP S. HENCH, Rochester, Minn.: One of my patients, an elderly woman, had had infantile paralysis as a child with resultant partial paralysis of one arm and hand. Despite persistent atrophy and arrested development of this hand she had slowly regained considerable use of it, probably 50 per cent normal. Years later definite Heberden's nodes developed on the fingers of her normal hand but not a sign of them appeared on the partially paralyzed extremity. Does this not suggest that some trophic factor, rather than mere age or trauma, plays a role in the production of Heberden's nodes?

DR. RALPH PEMBERTON, Philadelphia: There are many factors in the situation which have not been analyzed as yet and are possibly not susceptible to analysis. Thus when one considers familial incidence one must also consider topographic and geographic factors as well as traumatic and nutritional influences. However, there are probably few who can escape the conviction of at least occasional familial trends operative in both major aspects of the problem. In a series of 500 cases which my associate Dr. Bach and I have been studying, the evidence of hereditary influences is almost the same in the two major groups, namely atrophic 50 per cent, hypertrophic 42 per cent, mixed type 44 per cent. The relationship which Heberden's nodes bear to the syndrome of hypertrophic arthritis as a whole is perhaps not wholly clear. Dr. Stecher's remarks, however, coincide with the views of those who find it difficult to believe that hypertrophic arthritis is a manifestation of age and trauma alone.

DR. ROBERT M. STECHER, Cleveland: I hope that the more technical methods of genetics which Dr. Schweitzer has discussed can be applied to these data with profit. Tentatively Heberden's nodes seem, at the present time, to be inherited as a single chromosome factor which is sex influenced, being dominant in females and recessive in males. This lacks substantiation. Dr. Pemberton has mentioned other possible factors of etiology. Common environment is pretty well ruled out because Heberden's nodes occur in middle and late life long after sisters have ceased to live together. A common environment does not account for occurrence in three generations. Climate was not considered in the study on incidence. This study was confined to Cleveland, to people of the working class who attended public clinics. In the family studies, sisters were widely separated geographically. Social and economic differences were not considered in the incidence studies. However, I feel certain that inclusion of members of the leisure or wealthy class to the proportion in which they occur in the population in general would not materially affect the incidence statistics. My conclusions concerning trauma may seem rather dogmatic but they are based on extended inquiry from many affected persons. Traumatic arthritis of one finger or of several fingers on the same hand occurs after definite injury, a single episode of such severity that it is definitely recalled. I do not believe that it is proper to confuse trauma with ordinary use and function. Playing a piano or using a typewriter should not be considered trauma. Dr. Kling asks whether heredity plays a role in hypertrophic arthritis. The most that has been found in the literature is that hypertrophic arthritis runs in families or that 20 per cent of the families show more than one involved member. Such statements mean little because no information is available as to the proportion of involved to noninvolved persons in these families. Dr. Cecil has not told us how many siblings were born or lived to an age when Heberden's nodes might be expected in his family. If my theory is correct and the condition is recessive in males, we would expect only one half the men to be affected if the mother was heterozygous, all the men affected if the mother was also homozygous. If the father has Heberden's nodes, one would expect all his daughters to be affected regardless of the condition of the mother. I have seen one case similar to that described by Dr. Hench as well as another with peripheral nerve injury. The first of my patients had a daughter with Heberden's nodes, the second had a sister with Heberden's nodes. Three cases have been described in the literature of Heberden's nodes appearing after the patient suffered a hemiplegia. In these instances the healthy side alone was affected. Two patients had hemiplegias after Heberden's nodes had developed. After about a year's duration, no observable change has been noted in the nodes on the paralyzed side. I do not believe that trauma plays any part in such cases.

Local and Regional Analgesic Injections in the Treatment of Intractable, Nonsurgical Shoulder Conditions

DR. OTTO STEINBROCKER, New York: Analgesic solutions have been used for the past four or five years for diagnosis and treatment in arthritis and related musculoskeletal disease in the clinic in which I work. This report embraces our therapeutic experience with analgesic injections for the disabled shoulder. Before such treatment is undertaken complete examination, in doubtful instances necessary studies to rule out visceral pain, at least a tentative diagnosis, and a course of the usual medical and physical therapy are carried out as a matter of routine. Only a small percentage of affected shoulders were so refractory to other, accepted measures as to require analgesic injection. This treatment may be accomplished by (1) local, deep deposit of medication at the site of maximum tenderness, (2) regional supraclavicular brachial plexus block, (3) cervicodorsal paravertebral nerve block or (4) sympathetic (stellate ganglion) injection. The sympathetic approach is required occasionally for postherpetic and postamputation neuralgias. In the last few years we have had to resort to the paravertebral cervical block in only three cases.

Local injection at the site of maximum tenderness was employed for circumscribed fibrositis (fibromyositis, myofascitis, myositis) about the shoulder and neck, peripheral neuralgia and subdeltoid bursitis. In the majority of cases such treatment produced lasting effective results when the symptoms were due to referred pain. Local lesions were accompanied in some instances by secondary pain and tenderness in a surrounding halo or referred down the extremity. The secondary symptoms also responded when the peripheral source of trouble was correctly located and infiltrated. These circumscribed, peripheral disturbances often were eliminated by from one to ten injections of 2 to 15 cc. of 1 per cent procaine hydrochloride or equivalent aqueous solutions at intervals of from one to twenty-one days. In stubborn cases from 1 to 5 cc. of 2 per cent procaine base in oil was used. When repeated local injection failed, reconsideration of the diagnosis became necessary and brachial plexus block was utilized, when indicated.

We have found the supraclavicular brachial plexus block, with the Labat technic, a practical and effective procedure applied in our clinic without complication to ambulatory patients presenting intractable pain and disability of the shoulder region. The disorders treated by this method were diagnosed in the order of frequency as fibrositis of the periarticular and neck regions, osteo-arthritis of the cervicodorsal spine with referred symptoms, subdeltoid bursitis, rheumatoid arthritis (inactive), cervicobrachial neuralgia (due to pressure from fibrositis about the plexus or scalenus anterior involvement?) and osteo-arthritis of the shoulder joint (coraco-acromial, scapulohumeral). The conditions included in this group show a more or less identical symptom pattern dominated chiefly by pain referred down the extremity with limited abduction and rotation.

The severity of these symptoms in each case reflects the progress of the vicious cycle common in musculoskeletal disorder—pain, muscle spasm, postural deficiency, disability, deformity and trophic disturbances. According to our experience the cycle may be alleviated or abolished in selected cases by the use of the brachial plexus block with procaine solution. This technic was employed by us whenever possible in conjunction with manipulation, exercise and physical and medical measures which frequently had proved ineffective before blocking. Of seventy-six patients with intractable, usually chronic, shoulder

disorders, 73 per cent were greatly to completely relieved of symptoms and disability after from one to fourteen injections, averaging six, of 20 to 40 cc. of 1 per cent procaine solution or equivalent medication given at intervals of two to seven days.

DISCUSSION

DR. EZRA LIPKIN, Detroit: Following the publication of Dr. Steinbrocker's article in the *Annals of Internal Medicine* of June 1939 I injected 100 patients suffering from so-called rheumatic conditions with aqueous and oily solutions of procaine hydrochloride. Among these were forty-five patients with periarthritis of the shoulder, with negative x-ray appearances, who were treated by means of brachial block. The chief complaints were pain in the shoulder and arm, and limitation in abduction and external rotation. Following a number of regional injections of 1 to 2 per cent aqueous procaine hydrochloride solution—the average being three—there resulted either complete recovery or marked improvement in thirty-three of the forty-five patients, or 73 per cent—a figure which coincides exactly with that obtained by Dr. Steinbrocker. The period of observation extended up to eleven months. The anesthesia in the arm following the injection of the brachial plexus lasted from two to three hours and gave way to analgesia lasting from four to seven days or longer in some cases. Subsequent injections diminished the pain still further until there was complete remission or marked improvement of the symptoms. The one remarkable feature observed in the brachial block injections was the almost immediate relaxation of muscle spasm. I did not follow the injections with passive manipulation. Rather, the patient was encouraged to engage the arm in active exercise, which, because of freedom from pain, he was now able to perform. There were no untoward effects except for transient dizziness and numbness in the arm. When the brachial plexus is touched, the patient experiences a sudden, electric-like sensation in the arm. The solution is injected at this point. I used from 10 to 12 cc. of aqueous solution of procaine, although amounts up to 30 cc. have been recommended. Better results can be expected when the solution is injected directly into the nerve plexus rather than around it. Originally I employed the technic of Labat, injecting the solution in three areas, radiating from the single intradermal wheal 1 cm. above the midclavicle. To minimize trauma I reduced the number of points injected to one, namely, that aimed at the first rib. The results appeared to be as satisfactory as when the three injections were used, provided the brachial plexus is infiltrated, rather than the tissues around it.

DR. E. A. ROVENSTINE, New York: Nerve block or local infiltration procedures with analgesic solutions in painful nonsurgical conditions as a therapeutic or diagnostic measure is rapidly gaining a wide and more important usefulness. Local anesthetization is no cure-all for somatic pain. The procedure should never be substituted for an extensive attempt to discover the cause of pain and never be performed, unless as a diagnostic measure, until such an attempt has been made. As a more accurate neuro-anatomic approach to the problem of shoulder pain my associates and I block the suprascapular nerve at the lesser scapular notch. Our desire for blocking the nerve is based on the knowledge that its sensory components form a vital pathway for pain fibers from the scapulohumeral and acromioclavicular joints and periarticular structures about the shoulder joint. The articular and periarticular branches leave the nerve in the supraspinatus and infraspinatus fossae, so that to obtain interruption of all the sensory impulses transmitted over the nerve it is ideally blocked at the suprascapular notch. The details of the technic have been worked out in the anesthesia department at Bellevue and the favorable results seen have encouraged its continued use.

DR. J. ALBERT KEY, St. Louis: In my experience people who have analgesic injections for subdeltoid bursitis go home, the anesthesia wears off and then some of them may have terrible pain. With the use of nupercaine and oil it has been shown recently that the patient may get a prolonged anesthesia which goes on to actual degeneration of the nerve and permanent paralysis. My experience has been with the use of procaine in acutely inflamed bursae. Those can be cured. With the chronic conditions I have had relatively little luck, not anything like the percentage shown here.

DR. WILLIAM T. GREEN, Boston: More emphasis should be placed on diagnosis in making decisions as to the type of therapy to employ. In certain cases of back pain we have injected a solution of procaine into the skin over the area which was sensitive to palpation, followed by the disappearance of all tenderness. Most often the relief was temporary, but I have been amazed to see certain patients remarkably improved—though I do not recommend this as fundamental therapy. I do use local irrigations in the therapy of bursitis and tendinitis, as seen most frequently about the shoulder. After preliminary local anesthesia, two needles of 18 or 19 gage caliber are introduced into the calcific area, and through and through irrigation is carried out with physiologic solution of sodium chloride. It is my feeling that the excellent results obtained are due not to the injection of procaine hydrochloride on any analgesic basis but rather to the mechanical factors which are involved. Often calcific material may be obtained from such irrigation and in those cases in which we are unable to obtain it we lay particular stress in multiple needling of the involved area. The results in this procedure are satisfactory, particularly in the acute cases. In general, I am against analgesic injections, particularly of the type represented by a brachial plexus block, unless the process cannot be treated locally or the pain is intractable. It is my experience that passive motion is inferior to active motion or active guided motion in almost all instances.

DR. JOHN P. STUMP, New York: Dr. Steinbrocker has used the term "nonsurgical" in his title. That word means that his patients have been through the hands of internists, orthopedists and neurologists without relief before he has employed his method of nerve block. His results have been gratifying.

DR. A. S. GORDON, Brooklyn: What relation, frequency and association does Dr. Steinbrocker find between painful shoulders and local tender points along the cervical spine of the same side? What experience and success did he have in injecting other joints, particularly the knee joint?

DR. OTTO STEINBROCKER, New York: I consider it wise to avoid injecting directly into a nerve. Occasionally in the course of a routine block a nerve may be traumatized when the needle penetrates it and some later discomfort arises. It is advisable in ordinary therapeutic procedures to employ perineural injections. Of course following any type of block temporary local discomfort may occasionally appear shortly afterward or when anesthesia wears off. When it occurs, this reaction is transient and is thought to be due chiefly to the hyperemia produced. As far as my observation goes, I agree with Dr. Key on the treatment of acute bursitis. The methods I have described were applied to chronic bursitis. Proper diagnosis is a complex problem in many of these cases before blocking is done. It is at times difficult enough to decide on the wisdom and method of injection even after thorough diagnostic study. In some borderline situations, proper block may prove of diagnostic as well as therapeutic value. I try to determine the importance of mechanical factors before I begin treatment. Merely to inject a patient with obvious skeletal defects causing symptoms, or while he is receiving corrective therapy for poor body mechanics, is of course not advisable. Exceptions to this rule are individuals with persistent localized areas of pain and muscle spasm which delay improvement. Injecting such foci of irritation has been found a helpful adjunct, hastening response to other measures. Coronary and other cardiac disturbance complicated or obscured by parietal spine or shoulder symptoms may present difficult problems of diagnosis and treatment. If the complaints are not of cardiac origin, I use whichever procedure is indicated for the musculoskeletal condition. Unless moribund, the average cardiac patient takes block well and the resulting relief of discomfort helps in every way. If the pain is thought to be definitely cardiac in origin, particularly coronary, sympathetic (stellate) injection is indicated. If the origin of the symptoms remains doubtful and relief is imperative, local procedures are first used, then brachial plexus block and finally sympathetic injection. The problem of differential block in these conditions is not conclusive at this time. There are many phases of the subject of analgesic injections requiring further investigation and improvement but, correctly applied, those procedures now available are helpful in the relief and control of pain and disability in many conditions.

(To be continued)

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1930 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

American Journal of Diseases of Children, Chicago

60:783-1018 (Oct.) 1940

Prognosis in Postencephalitic Disorders. P. Heersema, Rochester, Minn. —p. 783.
Suspension Grasp Behavior of the Human Infant. Myrtle B. McGraw, New York.—p. 799.
*Hemolytic Disease in Infants. A. F. Abt, Chicago.—p. 812.
Blood Volume and Extracellular Fluid Volume of Infants and Children: Studies with Improved Dye Micromethod for Determination of Blood Volume. M. Robinow and W. F. Hamilton, Augusta, Ga.—p. 827.
Paranasal Sinuses from Birth to Late Adolescence: II. Clinical and Roentgenographic Evidence of Infection. M. M. Maresh and A. H. Washburn, Denver.—p. 841.
Intracutaneous Tests with Pertussis "Toxin" and Complement Fixation Tests in Whooping Cough. M. Weichsel, H. J. Rubin, P. Cohen and J. H. Lapin, New York.—p. 862.
*Disturbances of Hepatic Function in Icterus Gravis: Report of Two Cases. W. W. Zuelzer and J. A. Bigler, Chicago.—p. 873.
Levels of Sulfapyridine in Blood of Children Following Dosage by Body Weight. G. E. Cullen and Armine T. Wilson, Cincinnati.—p. 891.
Urine Collector for Female Infants. R. Cohen, Louisville, Ky., and M. L. Blatt, Chicago.—p. 897.
Adrenocortical Obesity in Children. T. M. Marks, Lexington, Ky.; J. M. Thomas, Omaha, and J. Warkany, Cincinnati.—p. 923.

Hemolytic Disease in Infants.—Abt reports three cases of hemolytic anemia in early infancy. The symptoms in one were observed at birth and in the other two at 4 months of age. A familial history could not be obtained. In early infancy the anemia is often a more pronounced symptom than icterus and is generally severe. The onset of the disorder may be insidious or it may occur as a severe hemolytic crisis and terminate fatally. Splenomegaly is usually of a considerable degree. When symptoms appear early, the first crisis is apt to be most severe. A severe crisis occurred in one of the cases. In the other two there were frequent crises which, though not so severe, necessitated transfusions at intervals of from three weeks to three months. Jaundice may be entirely absent even though there is indisputable evidence of blood destruction. The increase in reticulocytes is considerable. Increased fragility of the erythrocytes has been one of the usual criteria for the diagnosis of the condition. The leukocytes are generally normal or somewhat increased, and the platelets are usually within normal limits. An increase in normoblasts is generally observed. Bilirubinemia is always present. The icteric index is increased, and the indirect van den Bergh reaction is positive. Smears of the bone marrow obtained by sternal puncture reveal an increase in nucleated erythrocytes, a characteristic of hemolytic disease. General glandular enlargement is not usually observed in early infancy and was not present in the author's patients. There were no skeletal changes. Ocular lesions have not been reported in infancy. The crises of the disease show varying degrees of severity and different manifestations. Generally, infants manifest prodromal symptoms (lassitude, lack of appetite and fretfulness) followed by deepened jaundice and increased anemia. Usually during the periods of crisis the spleen enlarges and the urine becomes dark. Abdominal symptoms have not been characteristic of the condition in infancy. Occasionally crises are initiated by febrile attacks, when the symptoms are magnified and the infant may be extremely prostrate. Periodicity in the occurrence of crises is the rule. In one of the infants crisis occurred every three weeks, in another approximately every three months and in the third a single severe crisis occurred. The extent of jaundice and anemia vary considerably from attack to attack. The amount of urobilin in the urine is increased, especially after a crisis. Occasionally hemoglobinuria may be observed. The stools are normal but occasionally dark. Acholia is never present. Blood transfusion and serum are temporary therapeutic aids which effectively combat an acute crisis. Splenectomy is the permanent therapeutic measure, and its expectant benefits outweigh the operative hazards. Accessory splenic tissue should be searched for and removed at the time of operation. Two of the author's patients have successfully undergone splenectomy at the ages of 15 months and 2½ years, respectively. In the third there has been no recurrent crisis during the ten months following the initial attack, and no splenectomy has been performed.

Hepatic Function in Icterus Gravis.—Zuelzer and Bigler cite two cases to emphasize the importance of hepatic damage in certain cases of icterus gravis neonatorum. The two cases occurred in one family; one illustrates a protracted course resulting in cirrhosis and the other an acute phase of hepatic damage. Both cases were associated with an unusual derangement of carbohydrate metabolism on the basis of hepatic dysfunction which is rarely observed in infants. Both patients died, one after a survival of eight months which finally ended in cirrhosis and the other at the end of the first week of life with kernicterus. Severe fatty changes, hemosiderosis and deposits of bile pigment were found in the liver. No clinical or pathologic evidence of erythroblastosis was present in either case. The metabolic disturbances (insulin-refractory glycosuria, hyperglycemia, absence of ketosis and sensitivity to insulin) are interpreted by the authors on the basis of the pathologic observations as a manifestation of impaired hepatic glycogenesis. After insulin therapy, insulin-like reactions without associated hypoglycemia and anatomic damage to the brain were observed in one of the cases. The possibility of a direct toxic effect of insulin on the central nervous system in the absence of hypoglycemia is considered and a tentative explanation is submitted.

American Journal of Ophthalmology, St. Louis

23:1089-1198 (Oct.) 1940

Studies on Keratoconus Relative to Effect of Prolonged Application of Pressure. T. L. Terry and J. F. Chisholm Jr., Boston.—p. 1089.
Effect of Certain Physical and Chemical Stimuli on Caliber of Retinal Blood Vessels in Man. I. Puntenney, Chicago.—p. 1113.
Study of Practical Cycloplegia, with Special Reference to Use of Paredrine: Review of 341 Cases. E. J. Wenaas, W. H. Evans and R. E. Odom, Youngstown, Ohio.—p. 1123.
Concerning the Chamber Angle: III. Clinical Method of Goniometry. H. S. Gradle and H. S. Sugar, Chicago.—p. 1135.
*Homotransplantation of Preserved Cornea: Experimental Study. M. Fine, San Francisco.—p. 1140.
Inherited Eye Defect in Guinea Pig: Report of Further Anatomic Studies. H. L. Foust, Ames, Iowa.—p. 1146.
A Pressure Dressing. R. L. Pfeiffer, New York.—p. 1156.

Homotransplantation of Preserved Cornea.—Fine attempted to determine the relative merits of immediate and delayed transplantation of the cornea by controlled experiments on rabbits. Thirty-one animals were given partial penetrating transplants into normal corneas from eyes that had been enucleated at death and preserved for from twenty-four to fifty-two hours at a temperature of 4 C., as described by Filatov. The results obtained were compared with those of a control series of twenty-five rabbits in which homotransplants were performed with corneal tissue removed within twenty minutes after death. In the control group 52 per cent, or thirteen, of the operations resulted in grafts which were transparent to such a degree that the fundus could be seen through the graft. If one third of the transplant showed this degree of transparency, it was considered successful. In four of the thirteen clear grafts there were single narrow anterior synechiae. These did not result in vascularization or opacification of the transplants even after six months. In the thirty-one delayed transplantations (from twenty-four to fifty-two hours) there were ten clear grafts (32 per cent). Of sixteen operations with corneas preserved for twenty-four hours, seven resulted in transparent grafts and of fifteen operations with corneas preserved for forty-eight or more hours only three resulted in satisfactory grafts. The primary causes of opacification in corneal transplants are poor nutrition of the graft, infection, incarceration of the iris in the operative wound and vascularization. Secondary to these causes are poor adaptation of the margins of the graft to the host's cornea, marked early edema of the graft, corneal fistula, pressure from sutures on the surface of the graft, suture infection and folding of Descemet's membrane. When vascularization

occurred in fresh tissue grafts it resulted from the adherence of the iris to the posterior surface of the corneal wound or actual incarceration of the iris. In contrast, with preserved grafts vascularization for the most part was superficial and proceeded from the limbal loops as a result of degeneration of the superficial layers of the graft. Eight iris adhesions were encountered in the control group and five in the series of delayed transplants. The author concludes that until more conclusive evidence of the superiority of preserved cornea for keratoplasty is forthcoming the conservative surgeon will choose fresh tissue, if available, or tissue preserved for a minimal length of time.

American Journal of Physiology, Baltimore

130:421-612 (Sept.) 1940. **Partial Index**

Size of Extracellular Fluid Compartment Before and After Massive Infusions. A. M. Lands, R. A. Cutting and P. S. Larson, Washington, D. C.—p. 421.
Posttetanic Potentiation and Suppression in Muscle. L. Grumbach and D. T. Wilber, Ithaca, N. Y.—p. 433.
Anoxic Effects of High Oxygen Pressure on Smooth Muscle. J. W. Bean and D. F. Bohr, Ann Arbor, Mich.—p. 445.
Reduction of Blood Pressure of Hypertensive Dogs by Administration of Renal Extract. J. R. Williams Jr., Nashville, Tenn.; A. Grollman, Baltimore, and T. R. Harrison, Nashville, Tenn.—p. 496.
Distribution of Blood Perfusates in Capillary Circulation. B. W. Zweifach, New York.—p. 512.
Prolonged Action of Acidified Solution of Protamine Zinc Insulin. M. Sahjun, with assistance of A. Nixon, Detroit.—p. 521.
Comparison of Effects of Cold and Thyrotropic Hormone on Thyroid Gland. P. Starr and R. Roskelley, Chicago.—p. 549.
Mechanism of Depression of Serum Potassium Level by Epinephrine. P. S. Larson, Richmond, Va.—p. 562.
Mechanism of Action of Dicarboxylic Acids in Blood Coagulation. G. J. Martin, New York.—p. 574.
Hormone Influences on Carbohydrate Metabolism During Work. E. Asmussen, J. W. Wilson and D. B. Dill, Boston.—p. 600.
Further Observations on Total Chloride Content: Relationship Between Body Fat and Body Chloride. E. G. Weir, Washington, D. C.—p. 608.

Bulletin New York Academy of Medicine, New York

16:605-656 (Oct.) 1940

Aging of the Cardiovascular System. E. P. Boas, New York.—p. 607.
Histamine in Anaphylaxis and Allergy. L. Farmer, New York.—p. 618.
An American Precursor of Freud. A. A. Brill, New York.—p. 631.

California and Western Medicine, San Francisco

53:153-200 (Oct.) 1940

Obesity. E. H. Rynearson and Anne Whitcomb Sprague, Rochester, Minn.—p. 158.
Traumatic Appendicitis. G. K. Rhodes and W. D. Birnbaum, San Francisco.—p. 162.
Osteomyelitis of Bones of Face in Severe Diabetic: Recovery and Plastic Reconstruction. M. N. Hosmer, D. K. Burnham and A. D. Davis, San Francisco.—p. 165.
Infantile Eczema: Its Dermatologic Management. F. G. Novy Jr., Oakland.—p. 168.
Epilepsy: General Survey of Convulsive State. J. A. Cutting, Agnew.—p. 170.
Interpretation of Laboratory Examinations in Diagnosis of Infectious Diseases. C. S. Keefer, Boston.—p. 173.

Canadian Medical Association Journal, Montreal

43:305-404 (Oct.) 1940

A Decade of Pediatric Progress. A. Brown, Toronto.—p. 305.
Examination of the Recruit. A. R. Hagerman, Toronto.—p. 314.
Medical Aspects of the Air Force. R. W. Ryan, Regina, Sask.—p. 316.
Proposal for More Radical Treatment of Gunshot Wounds of the Brain. G. Horrax, Boston.—p. 320.
Fractures—Elastic Band Traction. S. D. McKinnon, Rouyn, Que.—p. 324.
Surgical Treatment of Flat Feet. G. L. Burke, Vancouver, B. C.—p. 327.
Congenital Hydronephrosis. A. Strasberg, Montreal.—p. 332.
Beneficial Action of Desoxycorticosterone Acetate in Uremia. H. Selye, Montreal.—p. 333.
Problems of the Adolescent Child. A. Goldbloom, Montreal.—p. 336.
Respiration During Anesthesia. M. D. Leigh, Montreal.—p. 340.
Nupercaine Spinal Anesthesia in Abdominal Surgery. A. R. Wilkins, Toronto.—p. 342.
Is Physical Examination of Lungs Worth While? J. D. Adamson, Winnipeg, Man.—p. 345.
People Who Are Always Complaining. A. H. Gordon, Montreal.—p. 349.
Intestinal Obstruction. W. A. Curry, Halifax, N. S.—p. 352.
Dermatologic Neuroses. W. R. Jaffrey, Hamilton, Ont.—p. 356.
Clinicopathologic Correlation Chart for Bright's Disease. S. W. Lippincott, Montreal.—p. 359.
Carcinoma of Cervix in the First Three Decades of Life. N. D. Hall, Phoenix, Ariz.—p. 362.
Essential Unsaturated Fatty Acids in the Relief of the Common Cold. E. M. Boyd and W. F. Connell, Kingston, Ont.—p. 365.

Connecticut State Medical Journal, Hartford

4:585-636 (Oct.) 1940. **Partial Index**

Physiology of Aviation and Medical Preparedness. J. F. Fulton, New Haven.—p. 590.
Aviation Medicine Today. W. B. Smith, Hartford.—p. 595.
Medical Aspects of Deep Sea Diving. C. W. Shilling, Washington, D. C.—p. 597.
Increasing Importance of Preventive Industrial Medicine. A. S. Gray, Hartford.—p. 600.

Delaware State Medical Journal, Wilmington

12:199-212 (Sept.) 1940

Medical Preparedness. B. Barnes, Seaford.—p. 199.
Acute Yellow Atrophy. H. G. Hadley, Washington, D. C.—p. 201.

Endocrinology, Los Angeles

27:533-706 (Oct.) 1940. **Partial Index**

Biologic Properties of Highly Purified Gonadotropin from Pregnant Mare Serum. H. H. Cole, R. I. Pencharz and H. Goss.—p. 548.
Nonspecific Augmentation with a Highly Purified Follicle Stimulating Hormone Fraction (Evans). F. Bischoff, Santa Barbara, Calif.—p. 554.
Influence of Chlorophyll on Activity of Gonadotropic Extracts Tested on Normal and Hypophysectomized Immature Female Rats. J. H. Leathem and U. Westphal, New York.—p. 567.
Specific Metabolic Principle of Pituitary. R. N. Feinstein and E. S. Gordon, Madison, Wis.—p. 592.
Further Purification of Growth Hormone of Anterior Pituitary. H. L. Fraenkel-Conrat, D. L. Meamber, Miriam E. Simpson and H. M. Evans, Berkeley, Calif.—p. 605.
Question of Presence of Thyroglobulin in Blood. L. I. Stellar and H. G. Olken, Boston.—p. 614.
Effect of Adrenalin in Peanut Oil and Adrenalin Pellets on Thyroid Gland of Guinea Pig and Rabbit. C. Goetsch, Rochester, N. Y.—p. 617.
Adrenalin-Induced Opacities of Lens in Rat. Caroline Tum Suden and L. C. Wyman, Boston.—p. 628.
Addison's Disease Treated by Implantation of Desoxycorticosterone Acetate Pellets. R. C. Moehlig, Detroit.—p. 633.
Corticosterone and Its Esters. M. H. Kuizenga and G. F. Cartland, Kalamazoo, Mich.—p. 647.
Production of Persistent Changes in Genital Organs of Immature Female Rats Treated with Testosterone. H. Selye, Montreal.—p. 657.
Colorimetric Estimation and Fractionation of Urinary Androgens: Assays of Normal and Pathologic Urines. E. J. Baumann and Nannette Metzger, New York.—p. 664.
Comparative Estrogenic Potency of Diethyl Stilbestrol. Estrone, Estradiol and Estriol. C. W. Sondern and J. L. Sealey, Kansas City, Mo.—p. 670.
Periodic Changes in Blood Estrogen. H. Lamport, New York.—p. 673.

Illinois Medical Journal, Chicago

78:285-376 (Oct.) 1940

Sulfapyridine Treatment of Pneumococcic Pneumonia. I. F. Volini and R. O. Levitt, Chicago.—p. 305.
Early Glaucoma. V. Wescott, Chicago.—p. 317.
Use of the Newer Insulins. T. D. Masters, Springfield.—p. 319.
Diagnosis and Treatment by the Proetz Method. H. L. Ford, Champaign.—p. 323.
Preeclampsia and Eclampsia at the Galesburg Cottage Hospital in the Last Decade. E. N. Nash, Galesburg.—p. 327.
Toxemias of Pregnancy at the Cook County Hospital. C. C. Doherty, Chicago.—p. 332.
Vitamin Therapy in Colon and Rectal Disease. C. J. Drueck, Chicago.—p. 337.
Prognosis in Juvenile Rheumatic Fever. S. Gibson, Chicago.—p. 341.
Diagnosis of Perforated Peptic Ulcer. L. River, Oak Park.—p. 344.
*Treatment of Psoriasis with Various Vitamin D Preparations. E. A. Thacker, New Orleans.—p. 352.

Vitamin D Preparations for Psoriasis.—Thacker used viosterol, crystalline vitamin D, a mixture of western fish oils, a special concentrated cod liver oil in capsules and a stock concentrated cod liver oil internally for the treatment of twelve persons afflicted with psoriasis. Concentrated cod liver oil in a vanishing cream base was applied to the psoriatic areas. The lesions of nine patients disappeared following treatment with the stock concentrated cod liver oil and the special concentrated cod liver oil in capsules. Two patients failed to respond to this therapy and the condition of one was slightly improved. The daily amount of vitamin D in the stock concentrated preparation used varied from 500 to 945 units per kilogram for the fifty-two to the ninety days during which it was given. The special concentrated cod liver oil in capsules required approximately twice this amount before the psoriasis disappeared. The first five persons treated have been free from psoriasis since treatment was terminated about one year ago. Psoriatic lesions failed to regress after the administration of seven or eight times as much vitamin D in the form of viosterol and crystalline vitamin D as that of the concentrated cod liver oil. The areas of psoriasis

also failed to respond to the mixture of western fish oils. Therefore it appears that cod liver oil contains an unidentified antipsoriatic factor in a greater quantity than is present in the other preparations used. The sequence in the disappearance of the lesions is a profuse coarse scaling which occurs generally within three weeks after treatment is begun followed by thinning, fading of the redness of the base and a fine branlike scaling. After the lesions are gone the formerly involved areas are not to be distinguished from uninvolved areas. Local application of concentrated cod liver oil had no effect on the disorder. Psoriasis is probably due to a metabolic disturbance, the nature of which is yet to be determined.

Journal of Nervous and Mental Disease, New York

92:429-568 (Oct.) 1940

Bilateral Cortical Thromboses: Report of Case. D. M. Palmer, Columbus, Ohio.—p. 429.
Hypoglycemic Epilepsy. L. J. Robinson, Palmer, Mass.—p. 442.
Degeneration of Basal Ganglions Associated with Olivopontocerebellar Atrophy. C. D. Aring, Cincinnati.—p. 448.
Vigilance and the Vitalistic Hypothesis. S. E. Jelliffe, New York.—p. 471.
Cerebellar Agenesis. H. S. Rubinstein and W. Freeman, Washington, D. C.—p. 489.

Journal of Nutrition, Philadelphia

20:197-304 (Sept.) 1940. **Partial Index**

Further Evidence of Mode of Action of Vitamin D. Margaret Cammack Smith and H. Spector, Tucson, Ariz.—p. 197.
Comparative Rate of Absorption of Some Natural Fats. H. J. Deuel Jr., Lois Hallman and A. Leonard, Los Angeles.—p. 215.
Calcium and Phosphorus Content of Certain Vegetables Grown Under Known Conditions of Fertilization. Ernestine Elmendorf and H. B. Pierce, Rochester, N. Y.—p. 243.
Metabolism of Citric Acid by Infants. A. H. Smith, D. J. Barnes, C. E. Meyer and M. Kaucher, Detroit.—p. 255.
Utilization of Calcium in Carrots, Lettuce and String Beans in Comparison with Calcium in Milk. J. B. Shields, B. W. Fairbanks, G. H. Berryman and H. H. Mitchell, Urbana, Ill.—p. 263.
Utilization of Calcium of Dicalcium Phosphate by Children. Elizabeth Kempster, Herta Breiter, Rosalind Mills, Beula McKey, Marie Bernds and Julia Outhouse, Urbana, Ill.—p. 279.
Pectic Enzymes: V. Fate of Pectins in Animal Body. Z. I. Kertesz, Geneva, N. Y.—p. 289.

Journal of Thoracic Surgery, St. Louis

10:1-130 (Oct.) 1940

Etiology of Thin-Walled Thoracic Cysts. A. V. S. Lambert, New York.—p. 1.
*Extrapleural Pneumothorax. E. C. Janes, D. B. Aitchison and A. Forsberg, Hamilton, Ont.—p. 8.
Extrapleural Pneumonolysis in Artificial Pneumothorax: Report of Thirty-Three Cases. J. S. Harter and A. A. Lilienthal, Sanatorium, Miss.—p. 14.
Bronchospirography: I. Description of Catheter and Technic of Intubation. W. A. Zavod, Mount Vernon, N. Y.—p. 27.
Id.: II. Application to Collapse Therapy: Preliminary Report. G. Leiner, M. Pinner, New York, and W. A. Zavod, Mount Vernon, N. Y.—p. 32.
Heart Pain. P. Heinbecker, St. Louis.—p. 44.
*Experiences in Surgical Treatment of Subacute Streptococcus Viridans Endarteritis Complicating Patent Ductus Arteriosus. A. S. W. Touroff and H. Vesell, New York.—p. 59.
Individual Ligation Technic for Lower Lobe Lobectomy. B. Blades and E. M. Kent, St. Louis.—p. 84.
*Experiences with Lobectomy and Pneumonectomy in Pulmonary Tuberculosis. F. S. Dolley and J. C. Jones, Los Angeles.—p. 102.

Extrapleural Pneumothorax.—Since November 1937 Janes and his co-workers performed extrapleural pneumothorax on seventy-seven patients. Fifteen have since had oleothorax. The interval between the operation and the replacement of air with oil has gradually decreased. The shortest interval was three months. Despite the fact that a bronchopleural fistula developed in one patient soon after the injection of oil, the staff is becoming convinced that the injection of oil to maintain permanent collapse is desirable in many cases. Because of inadequate collapse one patient had a second operation. The extrapleural space was deliberately combined with a preexisting intrapleural pneumothorax in eight patients. Four of these have made satisfactory progress. Bronchopleural fistulas developed in three and a tuberculous and pyogenic empyema with spread of the disease into the opposite lung in one. The empyema finally cleared and the space is satisfactory, but a cavity persists in the opposite lung. These eight cases suggest that it is not advisable to connect extrapleural and intrapleural spaces unless the location and extent of the disease command it. Three patients have had thoracoplasties since the extrapleural pneumonolysis. Eight of the seventy-seven patients have died; five deaths occurred within five or less weeks after operation and three were late postoperative deaths. The sputum was converted and the cavity closed in fifty of the sixty-nine living patients; the results were poor in the remaining nineteen, though three have subsequently improved following thoracoplasty. The authors conclude that unless with the further lapse of time the final result is not good the procedure should continue to be a useful collapse procedure.

Bacterial Endarteritis Complicating Patent Ductus Arteriosus.—Touroff and Vesell report four cases of subacute bacterial endarteritis complicating patent ductus arteriosus treated surgically. The rationale of the treatment is that ligation or excision often controls the bacteremia. For successful surgical eradication of the infection the vegetations should be confined to the ductus, and the ductus should be of sufficient length to permit excision. Unfortunately it is impossible to determine whether the vegetations are confined to the ductus, but certain information is available for the latter requirement. In the reported cases of operative uninfected patent ductus the length of the ductus varied from 0.5 to 1.2 cm. Practically all these operations were performed on children. It may be assumed that in adults the ductus would be larger. In three of the authors' cases the structure appeared to be of sufficient length to be divided and doubly ligated. If at operation the ductus is found too short the question arises whether operation is contraindicated. In the authors' first case the ductus was not completely excised but was divided and ligated as close to both orifices as possible. The interiors of the pulmonary artery and aorta were not inspected and the location of the vegetations was not known. The patient recovered from the infection following operation. This means that the vegetations were confined to the ductus and were completely excluded from the circulation by operation, or that they were also present in the pulmonary artery but healed quickly following closure of the arteriovenous shunt. If the latter were the case it appears that such spread would not contraindicate operation. If vegetations extend into the left side of the heart or the aorta, operation appears inadvisable as foci in these regions would continue to feed organisms into the peripheral circulation despite excision, division or ligation of the ductus. In the second case this was the sequence of events; therefore every effort should be made to determine involvement of the left side of the heart and aorta preoperatively. As subacute bacterial endarteritis superimposed on patent ductus is almost invariably fatal it appears justifiable to maintain that, barring the presence of major coexisting congenital cardiac anomalies or the generally poor condition of the patient, operation is contraindicated only in cases in which left-sided cardiac or aortic vegetations are present. The first of the authors' four adults recovered and has been well since operation nineteen weeks ago. The second patient was temporarily improved but the bacteremia persists seventeen weeks after operation. The third and fourth patients died of uncontrollable hemorrhage during operation. The recovery of one of the four patients affords little indication of the results regularly anticipated from such treatment, but since surgical therapy was successful in this case it should encourage others to give the method a thorough trial in the hope of reducing the mortality rate, which even the most optimistic observers place between 95 and 97 per cent.

Lobectomy and Pneumonectomy in Pulmonary Tuberculosis.—Dolley and Jones report seven cases of pulmonary tuberculosis, in four of which pneumonectomy and in three lobectomy was done. They advocate: (1) preliminary thoracoplasty with extrafascial apicolysis (while occasionally the final thoracoplastic stage may be included with the lobe or lung removal, they feel that this combined operation is usually inadvisable), (2) serial dissection of the hilar structures if technically possible, (3) the usual care in closure and burial of the bronchus, (4) immediate open drainage of the pleural cavity which by virtue of extensive thoracoplasty has become scarcely more than a broad slit, (5) painstaking removal by catheter suction of all possible infected material from the respiratory tract, (6) constant insistence during the early postoperative hours that the patient, with his pain controlled by analgesics, cough effectively and (7) minimal manipulation and instrumentation of the affected lobe or lobes preventing the purulent material within from

soiling the neighboring or contralateral pulmonary subdivisions. They believe that if, following thoracoplasty, it becomes apparent that a given patient is to remain disabled and his general condition warrants the surgical hazard and the technical difficulties are not too great, an attempt to remove the lobes involved is indicated. When bronchial stenosis is extreme or thick-walled cavities and extensive bronchiectasis exist which cannot be cared for adequately by extensive collapse or local compression this final measure is not justified until it is certain that nothing less radical will succeed. The final decision for lung removal is made after it has been found that extensive thoracoplasty is insufficient. Thoracoplasty is the preliminary procedure of choice. The authors are convinced that the removal of tuberculous lobes will become a reasonably safe and comparatively common procedure within the next few years. If the operative risks attain reasonable balance, lobectomy will be preferable to extensively necrotic lobe collapse. Contralateral spread is the most potential enemy at present. However, more and more potent weapons are being developed to combat it. Lobectomy should be limited at present to those patients for whom there is no other satisfactory recourse, and then only when the mediastinum and the chest wall have been stabilized and the residual potential empyema space has been minimized. Of their four patients undergoing pneumonectomy, two are dead and two will probably never regain their health. All had early or late contralateral spread. From the results in these patients the authors conclude that such patients should be prepared for pneumonectomy by thoracoplasty as more often than not the general condition of the patient is improved by thoracoplasty. Of the three patients on whom lobectomies of the right upper lobes were performed, two are well and able to work. The general condition of the third is excellent although her last sputum was positive. Toxic fatigue is notably absent in these patients, for their tuberculosis is gone with their lobes. In two, thoracoplasty preceded lobectomy; the postoperative course of all three was uncomplicated and in none was there a spread.

Laryngoscope, St. Louis

50:797-920 (Sept.) 1940

Otogenic Complications: Résumé and Discussion of Literature for 1939. L. G. Richards, Boston.—p. 797.
Observations on Conservation of Hearing. H. Newhart, Minneapolis.—p. 847.
The General Problem of Deafness in the Population. W. C. Beasley, Bethesda, Md.—p. 856.
Otitic Hydrocephalus: Report of Two Cases. J. J. Gitt, St. Louis.—p. 906.

Minnesota Medicine, St. Paul

23:681-754 (Oct.) 1940

An American Health Program. N. B. Van Etten, New York.—p. 681.
Roentgenologic Diagnosis of Intraspinal Protrusion of Intervertebral Disks. J. D. Camp, Rochester.—p. 688.
Treatment of Protruded Intervertebral Disks. J. G. Love, Rochester.—p. 692.
Intracranial Tumors: Study of 467 Histologically Verified Cases. A. B. Baker, Minneapolis.—p. 696.
Small Carcinomatous Gastric Lesions Simulating Chronic Benign Ulcer: Present Status of Differential Diagnosis and Treatment. G. B. Eusterman, Rochester.—p. 703.
*Surgical Treatment of Gastric Cancer Masquerading as Benign Disease. W. Walters and W. H. Cleveland, Rochester.—p. 709.
Indications for Use of Iron in Treatment of Anemias. P. F. Eckman, Duluth.—p. 712.
Toxic Effects of Carbon Tetrachloride: Report of Case. W. S. Hagen, H. A. Alexander and T. A. Peppard, Minneapolis.—p. 715.

Surgical Treatment of Gastric Cancer Masquerading as Benign.—Walters and Cleveland believe that too often gastric and duodenal ulcers are grouped under the misleading title of "peptic ulcer" and their inherent dissimilarities neglected and thus not recognized as occurring in individual types of tissue in which pathologic reaction and response to medical and surgical treatment is different. A large chronic gastric ulcer (more than 2.5 cm. in diameter) in a patient more than 40 years of age, especially if perforation, obstruction or hemorrhage has been present, or one on the greater curvature or near the pylorus usually should be removed surgically without delay, as few of these lesions respond to medical treatment and many may be carcinomatous. The small gastric ulcer which has failed to heal or has recurred under adequate medical management should be removed surgically, for if the lesion is malignant it is frequently of high degree. In a recent study at the Mayo Clinic of 100 consecutive small, presumably benign, gastric lesions removed, nineteen were found to be carcinomatous on pathologic examination. Partial gastrectomy of the Pólya type of end to side anastomosis posterior to the colon is the best surgical procedure for gastric ulcer. If the lesion proves to be malignant on microscopic examination its removal by partial gastrectomy gives the patient the best chance of cure, for it removes the lymphatic regions of the portion of the stomach removed and in the adjacent gastrocolic and gastrohepatic omentums, which might harbor malignant cells from the original lesion. When partial gastrectomy cannot be performed safely, less radical methods, such as excision of the ulcer with gastro-enterostomy or occasionally by excising the ulcer alone, are indicated. If possible the lesion should always be removed, but if the condition of the patient is such that its removal is impossible without too great a risk, a procedure should be done which sufficiently alters the conditions that healing of ulceration may be anticipated. The results from well chosen surgical procedures for gastric ulcers are among the best in surgery. Forty-three of sixty-two patients with benign gastric ulcer had partial gastrectomy with one death. Most of these procedures were of the posterior Pólya type. Among another 131 patients with gastric ulcer who had the posterior Pólya type of resection eighty of eighty-five who responded to a questionnaire were in excellent health without distress, while five were in good health with only slight occasional distress. The high location of a gastric ulcer should not deprive patients of surgical treatment when such management is indicated; also such lesions may be more accessible than the x-ray examination would indicate. Preoperative differential diagnosis between a benign and a malignant ulcer is difficult and the x-ray observation that a gastric ulcer is present does not exclude the possibility that it may be malignant.

Missouri State Medical Assn. Journal, St. Louis

37:409-454 (Oct.) 1940

Studies in Blood Coagulation Disturbances. H. N. Sanford, Chicago.—p. 409.
Functional Menstrual Disturbances. E. D. Plass, Iowa City.—p. 418.
Circulatory Mechanism Disorders: Recognition and Management of the Commoner Sudden Disturbances. G. Herrmann, Galveston, Texas.—p. 421.
Food Allergy. H. J. Rinkel, Kansas City.—p. 428.
The St. Louis Pneumonia Control Program: Statistical Evaluation of Various Forms of Therapy. E. Sigoloff, St. Louis.—p. 431.
Id.: Epidemiologic Aspects. S. E. Sulkin, St. Louis.—p. 435.
Twenty-Eight Years with Ether. O. O. Smith, St. Louis.—p. 440.
Premarital Examination Laws. L. D. Cady, St. Louis.—p. 443.

Review of Gastroenterology, New York

7:373-456 (Sept.-Oct.) 1940

Effect of Parathyroid Hormone and of Activated Ergosterol on Gastric Secretion in Dog. B. P. Babkin, Montreal.—p. 373.
Plea for More Frequent Use of Duodenal Alimentation in Treatment of Peptic Ulcers. M. Einhorn, W. H. Stewart, F. Huber and C. W. Breimer, New York.—p. 383.
Symptoms, Diagnosis and Treatment of Chronic Cardiospasm. E. B. Freeman, Baltimore.—p. 385.
Early Diagnosis of Gastric Cancer. S. Cytronberg, Mexico City, Mexico.—p. 391.
Standardized Measures for Study of Cecum, Special Reference to Undescended Cecum. A. X. Rossien, Kew Gardens, N. Y., and A. J. Cantor, Flushing, N. Y.—p. 399.
Indications and Contraindications of Medical Treatment in Cholecystitis and Duodenal Ulcer. T. Miller, Dallas, Texas.—p. 403.
Indication for Operation in Acute Cholecystitis. J. L. Ransohoff and H. Topolofsky, Cincinnati.—p. 412.
Surgical Treatment of Gallbladder Disease. R. Zollinger, Boston.—p. 420.
Secretin Test as Aid in Differential Diagnosis of Steatorrheas: Report of Fourteen Cases. J. S. Diamond, S. A. Siegel and S. Myerson, New York.—p. 429.

West Virginia Medical Journal, Charleston

36:441-488 (Oct.) 1940

Acute Surgical Lesions of Abdomen. I. Abell, Louisville, Ky.—p. 441.
Management of Urinary Infections in Children. R. M. Tyson, Philadelphia.—p. 451.
Androgens in Medicine. L. C. McGee, Elkins.—p. 458.
Diverticulum of Female Urethra with Calculi: Case Report. G. G. Irwin, Charleston.—p. 470.
Aortic Aneurysm: Case Report. A. C. Woofter and O. B. Barker, Parkersburg.—p. 472.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

British Medical Journal, London

2:437-478 (Oct. 5) 1940

The Journal and the Profession: Some Memories. D. Power.—p. 437.
*Cerebrospinal Fever: Analysis of 124 Cases. R. W. Cushing.—p. 439.
Examination of the Heart in Recruits. G. Bourne.—p. 442.
Colorimetric Standards for Emergency Estimations of Certain Constituents of Blood and Cerebrospinal Fluid. E. J. King.—p. 445.
Recent Advances in Treatment of Gonorrhea. D. J. Mackinnon.—p. 448.

Cerebrospinal Fever.—Cushing states that from Nov. 11, 1939, to May 26, 1940, 124 patients with cerebrospinal fever differing from that seen in 1914 to 1918 were admitted to the Military Isolation Hospital, Aldershot, and treated with benzylsulfanilamide derivative by the intravenous route. The onset of the fever was sudden. Many patients went to bed feeling quite well and awoke in the morning with intense headache, frequently accompanied by vomiting. Incubation appeared to be from twenty-four to forty-eight hours. Some patients had various symptoms, especially sore throat or general malaise lasting one to seven days before the appearance of the headache. The fulminating septicemic type was even more sudden than this. Twenty-eight of the cases were classified as slight, 49 as moderate, 41 as severe and 6 as fulminating septicemic. The clinical picture was that of an extremely ill patient with the anxious expression of one in distressing pain. The lips and cheeks were pale and gray, showing a definite toxemia with much blood destruction. The skin was damp with perspiration. The most characteristic and distressing symptom was the intense and intolerable headache. The removal of from 30 to 50 cc. of cerebrospinal fluid would relieve the distressed condition immediately. The next important sign (in 116 cases) was nuchal rigidity with intense pain on attempting to approximate the chin to the chest. Vomiting was fairly constant and lasted from one to four days. During this stage benzylsulfanilamide derivative was valuable. Often the patient's mental condition was abnormal, presenting considerable cerebral irritation and mental depression. The temperature was no guide in establishing a prognosis or determining the severity of the case. Only 3 patients had a temperature of 103 F. on admission; 102 had less than 100 F. The pulse rate was much more indicative of the severity of the infection. A slow pulse rate was evident only in cases of increased pressure of the cerebrospinal fluid or in full dosage of the sulfonamide drug used. The reflexes followed no definite pattern. The patients with the fulminating type of fever showed meningeal signs; but the predominant clinical picture was acute generalized toxemia, and some were presumably septicemic in nature. In others the clinical picture simulated typhoid with pyrexia and a macular rash and in these cases the meningococcus could be isolated by blood culture. Within twenty-four or even twelve hours after the initial intravenous injection of benzylsulfanilamide derivative and lumbar puncture the temperature fell to normal, the intensity of the headache was diminished and in some cases entirely eliminated, nuchal rigidity lessened and vomiting ceased or lessened in persistence and severity. By this time sulfapyridine given orally in diminishing amounts caused no vomiting. Treatment was stopped in eight or nine days and the patient proceeded to uneventful recovery, was allowed up in from thirteen to twenty-one days and after four or five weeks of hospital treatment was discharged on five weeks' convalescent leave. After five weeks of convalescence 25 patients declared themselves perfectly well and fit, 48 complained of early fatigue on exercise and occasional dizziness, 6 complained of pain in the back and 42 exhibited effort syndrome in varying degrees of severity. Forty-eight were recommended for a period of light duty under the supervision of a regimental medical officer and 25 were returned to their unit as "fit for duty." For the others further convalescent treatment was recommended before their return to supervised light duty. The majority of the patients were young militiamen who contracted the infection after a short period of service. There were four deaths. Since May there have been eleven more admissions, and as no other deaths have occurred the total mortality rate is brought down to 2.9 per cent. Benzylsulfanilamide, 20 cc. of a 5 or 10 cc. of a 10 per cent solution, is injected intravenously into one of the veins over the antecubital fossa. This can be repeated in four to eight hours, according to the severity of the case, and may be continued for three or four days until the patient's initial signs and symptoms disappear. The results were so constantly good and the effects so speedy that the drug is recommended for routine treatment at the outset in all cases except perhaps the mildest. Once the diagnosis is made, no further lumbar punctures are performed unless signs of intracranial pressure arise.

Quarterly Journal of Medicine, Oxford

9:193-246 (July) 1940

Poisoning by Methyl Mercury Compounds. D. Hunter, R. R. Bomford and Dorothy S. Russell.—p. 193.
*Liver Function in Thyrotoxicosis. N. F. Maclagan and F. F. Rundle, with experimental data by H. B. Collard, F. H. Mills and F. F. Rundle.—p. 215.
*Action of Parasympathetic-Mimetic Drugs in Asthma. H. H. Moll.—p. 229.

Liver Function in Thyrotoxicosis.—Maclagan and his colleagues determined the hepatic function of forty-one patients with hyperthyroidism by means of a modified galactose tolerance test. Thirty of the patients showed definite impairment of hepatic function, and the remaining eleven gave results in the upper normal range (galactose index above 68). Clinical grading of the cases as severe, moderate and mild showed a definite relationship between the galactose index and the severity of the disorder. A significant correlation existed between the galactose index and the basal metabolic rate of untreated patients. Rest and iodine therapy had little effect on the galactose index, but in most instances thyroidectomy produced a prompt fall to normal values. Some residual impairment was demonstrated in a few cases studied at long intervals after thyroidectomy for severe hyperthyroidism. Daily subcutaneous administration of thyroxine to rabbits for periods up to seventeen days produced a marked impairment of tolerance to galactose injected intravenously. The livers of these animals also showed severe focal necrosis when examined microscopically. The galactose tolerance depends essentially on hepatic glycogenesis and this is the hepatic function which is particularly impaired in thyrotoxicosis and therefore the test reveals the typical disorder of the liver in this disease. It is possible that the toxic effect of the thyroid hormone on the liver is connected with its action in interfering with glycogenesis. The authors' data suggest that, when the galactose index is markedly high, structural hepatic damage is probably present. When the galactose index is only moderately raised their data do not show whether the change is a functional one or whether organic lesions are also present. The fact that normal limits were usually regained in fourteen days favors the functional explanation, and the fact that the iodine therapy has little or no effect suggests an organic cause. The galactose index provides an additional physical sign of hyperthyroidism.

Action of Parasympathetic-Mimetic Drugs in Asthma.—Moll observed the effect of mecholyl (acetyl-beta-methylcholine chloride) on twenty-eight persons with asthma and thirty-eight control subjects (normal medical students and nonasthmatic hospital patients with or without other types of respiratory disorders). He finds that the mecholyl test does not help to differentiate the different types of asthma, and patients with reflex asthma or persons in whom attacks are released psychogenically through nervous channels are not more susceptible to mecholyl than persons with infective or allergic asthma. However, the test may be helpful in the diagnosis between true asthma and respiratory neurosis, and especially hysterical hyperpnea: bronchospasm occurs in the former instance but not in the latter. The twenty-eight asthmatic subjects almost invariably responded with respiratory symptoms, which varied in intensity from slight wheeziness to severe asthma-like attacks. The control subjects showed general signs of parasympathetic stimulation (flushing, sweating, lacrimation and salivation) but chest symptoms did not develop. The tropism of choline derivatives for the bronchial system appears to be due not to a state of increased sensitivity of

the whole of the parasympathetic system (vagotonia) but only of the bronchial nerve endings or of the bronchial muscle itself. Pulmonary damage is an essential factor in determining the abnormal bronchial response. No matter how mild or infrequent the attacks of asthma may be, an asthmatic subject is nearly always susceptible to the drug. The asthma-like attack produced by choline derivatives is similar to, but probably not identical with, spontaneous asthma.

Schweizerische medizinische Wochenschrift, Basel

70:849-872 (Sept. 7) 1940. **Partial Index**

*Symptom of Narrowed Intervertebral Disk. H. Schaer.—p. 849.
*Primary Inoculation Tuberculosis of Vulva Caused by Cohabitation. M. Schmid.—p. 852.
Symptomatology and Therapy of Thyrogenic Migraine. E. I. Steuer.—p. 853.

Narrowed Intervertebral Disk.—Schaer directs attention to the fact that narrowing of the intervertebral disk is frequently encountered in diseases of the vertebral column. It is observed as an accompanying symptom of numerous degenerative changes of the intervertebral disk or of the adjoining vertebral bodies in the frequent spondylosis deformans. It is seen as a characteristic sign in juvenile kyphosis, in kyphosis of the aged and in osteoporosis of the aged. In all these cases the narrowing involves all or several of the disks. The narrowing of an isolated intervertebral disk occurs much less frequently and is difficult to diagnose. The author describes several cases in which this symptom was present and discusses the underlying pathologic process. Isolated narrowing of an intervertebral disk is due either to a reduction in its volume as the result of primary degeneration of the disk itself (osteochondrosis) or to pathologic processes in the surrounding tissues. The narrowing is found chiefly as an early roentgenologic symptom of tuberculous spondylitis. It is the result of the breaking through of the still intact intervertebral disk into a circumscribed diseased area of the adjoining vertebra. The deformation resulting from this breaking through leads to a seeming contraction, which at times is regular and at others irregular and which is frequently accompanied by a dorsal displacement of the vertebra above it. This early symptom of tuberculous spondylitis corresponds to the anatomic stage of the cavernous destruction of the vertebral body, a fact that has to be considered in estimating the age of a tuberculous process in the vertebral column.

Primary Inoculation Tuberculosis of Vulva.—Schmid maintains that in order to designate an extrapulmonary tuberculosis as a primary complex it is necessary to demonstrate the characteristics of the primary complex, namely a tuberculous inflammatory lesion at the portal of entry with swelling and caseation of the regional lymph nodes, and to rule out the existence of a tuberculous process in other parts of the body. The literature on primary extrapulmonary tuberculosis contains cases developing from ritual circumcision, from the injection of incompletely sterilized milk, from the piercing of ear lobes for the attachment of earrings, from injuries of the feet while walking barefoot, from contact with tuberculous cattle (in veterinaries and butchers) and from the kiss of patients with pulmonary tuberculosis. The possibility of a primary tuberculosis caused by cohabitation was demonstrated in guinea pigs in 1920. Five human cases of primary inoculation tuberculosis by cohabitation have been reported since 1929. The author reviews these cases and presents a detailed report of a case of his own. A woman aged 28 developed an ulcer at the attachment of the hymen a short time after defloration. Later the inguinal glands became sensitive to pressure. The diagnosis was undecided between syphilis, venereal lymphogranuloma and simple defloration ulcer. Repeated Wassermann and Frei tests were negative. Examination for gonorrhea was likewise negative. Some time later one of the inguinal glands perforated spontaneously, but the pus exuding from this gland contained no bacteria. Later several lymph nodes were excised and the microscopic examination disclosed caseous tuberculosis. Under a strengthening regimen, tuberculin therapy and local roentgen irradiation the lymph nodes decreased in size, the general condition improved and the vulval ulcer healed. Pirquet's tuberculin reaction was still strongly positive at the time of the patient's dismissal from the hospital. The primary tuberculous complex on the vulva induced an examination of the cohabitation partner. This revealed tuberculosis of the prostate and of the seminal vesicles in a man who previously had been treated for tuberculosis of the bones.

Archivos de Oftalmología de Buenos Aires

15:377-428 (Aug.) 1940. **Partial Index**

Encephalography in Diagnosis of Chiasmal and Hypophysial Lesions. M. Balado and M. F. Oribe.—p. 377.
*Sulfanilamide in Trachoma. J. Lijo Pavia.—p. 400.

Sulfanilamide in Trachoma.—Lijo Pavia, head of the Argentine committee for the prevention of blindness, reports on sulfanilamide treatment of trachoma of three groups of twenty-six patients each. These groups included children and adults. The disease was of the first, second and third degrees. The patients were not hospitalized; they remained at home in order not to be exposed to the sun's rays. The drug (azosulfamide) was administered on fifteen consecutive days in a daily dose of 0.02 Gm. for each kilogram of body weight for the first five days, 0.03 Gm. for the next five days and 0.04 Gm. for the last five days. The treatment was well tolerated. Photophobia, lacrimation, blepharospasm and conjunctival hyperemia showed improvement within the first five days of the treatment and generally disappeared in the course of it. Edema was reabsorbed, the pannus cleared and the transparency of the cornea and vision improved. The nodules became smaller and in some cases disappeared in the course of treatment or sometime after. Six patients were observed for three months after discontinuation of the treatment. Some of the patients instilled a drop of a 0.5 per cent zinc solution or an eyewash of a weak solution of mercuric oxycyanide. All the nodules had diminished in number and size and in some instances had disappeared. The author believes that sulfanilamide has an immediate therapeutic action on trachoma and a late action on the remaining nodules, with the probable exception of cases in which there are advanced forms of the disease. The patients had the treatment too recently to enable one to predict the future behavior of the disease and whether or not the results will be permanent.

Nordisk Medicin, Gothenburg

7:1303-1336 (Aug. 3) 1940

Roentgen Diagnosis in Acute Abdominal Cases. G. Petrén.—p. 1303.
*Hemorrhagic Disease in Newborn: Hypoprothrombinemia in Newborn. L. Salomonsen.—p. 1309.

Hypoprothrombinemia of Newborn.—Salomonsen states that all hemorrhagic conditions of the newborn are accompanied by a delayed coagulation time which depends on a hypoprothrombinemia due to vitamin K deficiency probably originating because of deficient formation of vitamin K in the sterile intestinal canal of the newborn. He asserts that giving a little cow's milk as early as from the second hour of life will almost wholly prevent this physiologic disturbance in coagulation.

Hospitalstidende

*Two Cases of Constitutional Infantile Anemia. P. Hjorth.—p. 1313.
Animal Experimentation on Heat Treatment of Malignant Tumors. K. Overgaard and H. Okkels.—p. 1317.

Constitutional Infantile Anemia.—Hjorth presents the cases of a brother and a sister, in both of whom, at the age of 8, a grave hyperchromatic anemia developed in the course of a few months with leukopenia and thrombopenia and hemorrhagic diathesis. There was hypoplasia, but not aplasia, of the bone marrow, also hypoplasia of the thymus and, in the boy, hypoplasia of the testes. Congenital bone deformities were present, clubfoot in the boy, bilateral luxation of the hip in the girl. The children were kept alive for two and a half years and four years respectively by means of blood transfusions, thirty in each case; no other treatment was of avail. A marked disposition to congenital bone deformities was established in the mother's family, and one member of the father's family was born without thumbs. These cases resemble five cases reported in the literature (Fanconi, Uehlinger and van Leewen) and designated by Uehlinger and van Leewen as "congenital infantile anemia."